L Number	Hits	Search Text	DB	Time stamp
1	65	(dibenz or dibenzo) with (azepin or diazepin)	USPAT; US-PGPUB	2003/09/04 11:56

EAST

10/076,574

09/ 076,574

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NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Feb 24	PCTGEN now available on STN
NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
NEWS 7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 8	Mar 24	PATDPAFULL now available on STN
NEWS 9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	AUG 22	Indexing from 1927 to 1936 added to records in CA/CAPLUS
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 15	Apr 28	RDISCLOSURE now available on STN
NEWS 16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 18	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 29	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 30	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 31	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 32	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 33	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 34	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS 35	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 36	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 37	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation
NEWS 38	AUG 18	Simultaneous left and right truncation added to ANABSTR

09/ 076,574

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 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

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                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.21       0.21

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STRUCTURE FILE UPDATES:    1 SEP 2003  HIGHEST RN 577691-42-0
DICTIONARY FILE UPDATES:   1 SEP 2003  HIGHEST RN 577691-42-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

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Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L1 HAS NO ANSWERS
L1              STR
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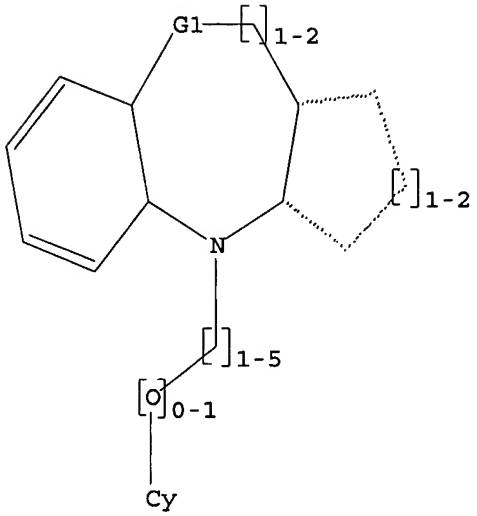

G1 C,N

Structure attributes must be viewed using STN Express query preparation.

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FULL SCREEN SEARCH COMPLETED - 301636 TO ITERATE

100.0% PROCESSED  301636 ITERATIONS                          1920 ANSWERS
SEARCH TIME: 00.00.09

L2          1920 SEA SSS FUL L1

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                     148.95     149.16

FILE 'CAPLUS' ENTERED AT 13:25:39 ON 03 SEP 2003
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FILE COVERS 1907 - 3 Sep 2003  VOL 139 ISS 10
FILE LAST UPDATED: 1 Sep 2003  (20030901/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
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         49428 PROPIONIC
L4           12 L3 AND PROPIONIC

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YOU HAVE REQUESTED DATA FROM 12 ANSWERS - CONTINUE? Y/(N):y

L4   ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2000:756706  CAPLUS
DOCUMENT NUMBER:          133:321882
TITLE:                    Preparation of substituted fused imidazoles for
                          treatment and/or prevention of diseases and disorders
                          related to the histamine H3 receptor
INVENTOR(S):              Dorwald, Florencio Zaragoza; Andersen, Knud Erik;
                          Jorgensen, Tine Krogh; Peschke, Bernd; Wulff, Birgitte
                          Schjellerup; Pettersson, Ingrid; Rudolf, Klaus;
                          Stenkamp, Dirk; Hurnaus, Rudolf; Muller, Stephan
                          Georg; Krist, Bernd
PATENT ASSIGNEE(S):       Novo Nordisk A/S, Den.; Boehringer Ingelheim
                          International, G.m.b.H.
SOURCE:                   PCT Int. Appl., 169 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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     WO 2000063208      A1   20001026       WO 2000-DK179    20000413
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             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW,
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             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1173438         A1   20020123       EP 2000-918714   20000413
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     JP 2002542245      T2   20021210       JP 2000-612298   20000413
PRIORITY APPLN. INFO.:                  DK 1999-508      A  19990416
                                        DK 1999-1345     A  19990922
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OTHER SOURCE(S):          MARPAT 133:321882
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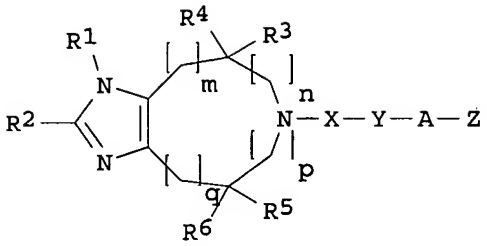

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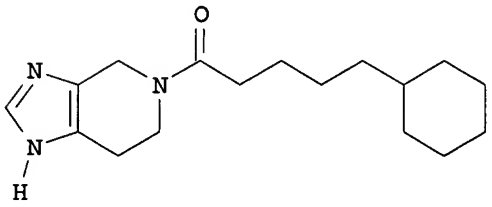


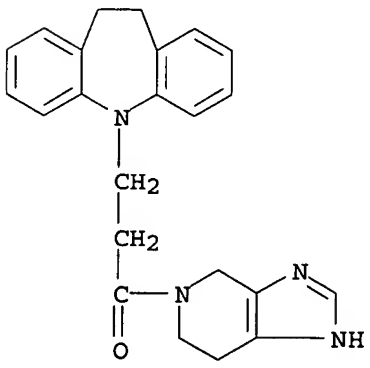
II

AB The title compds. [I; R1 = H, a functional group which can be converted to H in vivo; R2 = H, alkyl, halo, etc.; R3-R6 = H, CO2H, alkoxycarbonyl, etc.; m, n, p, q = 0-2; X = a bond, CH2, CO, etc.; Y = a bond, O, NR12 (R12 = H, alkyl, aryl, etc.); A = a bond, alkylene, alkenylene, etc.; Z = R13, OR13, SR13, etc. (R13 = H, alkyl, aryl, etc.)], useful for the treatment and/or prevention of diseases and disorders related to the histamine H3 receptor (more particularly, useful for the treatment and/or prevention of diseases and disorders, in which an interaction with the histamine H3 receptor is beneficial), were prepd. and formulated. E.g., treatment of 5-cyclohexylpentanoic acid with carbonyldiimidazole in DCM followed by addn. of 4,5,6,7-tetrahydroimidazo[4,5-c]pyridine in DCM afforded 24% II. Compds. I are effective at 0.05-10 mg/kg/day.

IT **303019-87-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted fused imidazoles for treatment and/or prevention of diseases and disorders related to the histamine H3 receptor)

RN 303019-87-6 CAPLUS

CN 1H-Imidazo[4,5-c]pyridine, 5-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)-1-oxopropyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:613895 CAPLUS
DOCUMENT NUMBER: 131:243192
TITLE: Preparation of novel heterocyclic compounds (dibenzazepines and analogs) for treatment of painful and inflammatory conditions
INVENTOR(S): Hohlweg, Rolf; Jorgensen, Tine Krogh; Andersen, Knud Erik; Olsen, Uffe Bang; Polivka, Zdenek; Sindelar, Karel
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947517	A1	19990923	WO 1999-DK135	19990316
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6214816	B1	20010410	US 1999-266236	19990310
AU 9928259	A1	19991011	AU 1999-28259	19990316
EP 1071679	A1	20010131	EP 1999-908771	19990316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002506863	T2	20020305	JP 2000-536712	19990316

PRIORITY APPLN. INFO.: DK 1998-366 A 19980317
US 1998-78954P P 19980323
WO 1999-DK135 W 19990316
OTHER SOURCE(S): MARPAT 131:243192
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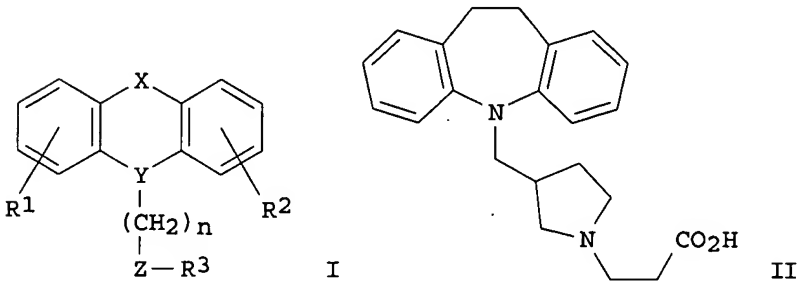


I II

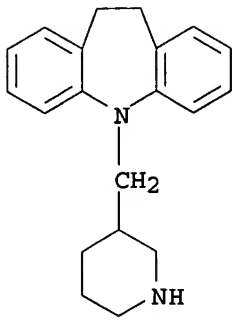
AB The invention relates to novel N-substituted azaheterocyclic compds. I [wherein X = o-C6H4, O, S, (un)substituted CH2, CO, CH2CH2, CH:CH, NHCO, CH2O, CH2S, etc.; Y = trivalent groups N(CH2), C(:CH), or CH(CH2) (where the ring atom is 1st and the sidechain atom 2nd); R1, R2 = H, halo, CF3, OH, C1-6 alkyl or alkoxy; Z = nucleus selected from piperidine,

(alkyl)piperazine, (thio)morpholine, pyrrolidine, tetrahydro(iso)quinoline, or aminocyclohexane; R3 (bound at N atom of Z) = (CH2)mOH or (CH2)pCOR4; m, p = 1-4; R4 = OH, NH2, NHOH, or C16 alkoxy; n = 0-2], or salts thereof. The invention also relates to methods for prepn. of the compds., to compns. contg. them, and to their use for the clin. treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role by eliciting neurogenic pain or inflammation. Also disclosed is use of the compds. for treatment of indications caused by or related to the secretion and circulation of insulin antagonizing peptides, e.g., non-insulin-dependent diabetes mellitus (NIDDM) and ageing-assocd. obesity. For instance, 10,11-dihydro-5H-dibenzo[b,f]azepine underwent a sequence of: (1) N-alkylation by 1-benzyl-3-(chloromethyl)pyrrolidine (15%), (2) hydrogenolytic debenzylation (78%), N-alkylation by BrCH2CH2CO2Et (89%), and finally alk. hydrolysis (69%), to give title compd. II, isolated as the hydrochloride. In the histamine-induced rat paw edema test, II.HCl gave 56% inhibition at 1.0 mg/kg i.p.

IT **13564-24-4P**, 3-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]piperidine **13564-30-2P**, 4-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]piperidine **244196-38-1P**, 5-[(1-Benzylpyrrolidin-3-yl)methyl]-10,11-dihydro-5H-dibenzo[b,f]azepine **244196-39-2P**, 5-(Pyrrolidin-3-ylmethyl)-10,11-dihydro-5H-dibenzo[b,f]azepine **244196-40-5P**, 3-[3-[(10,11-Dihydro-5H-dibenzo[b,f]azepin-5-yl)methyl]pyrrolidin-1-yl]**propionic** acid ethyl ester **244196-41-6P**, 2-[2-[(10,11-Dihydro-5H-dibenzo[b,f]azepin-5-yl)methyl]morpholin-4-yl]acetic acid ethyl ester **244196-43-8P**, 3-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)carbonyl]-1-benzylpiperidine hydrogen oxalate **244196-44-9P**, 3-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-1-benzylpiperidine **244196-45-0P**, [3-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-1-piperidyl]acetic acid ethyl ester **244196-47-2P**, 1-Methylsulphonyl-2-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]piperidine **244196-48-3P**, 2-[3-(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]piperidine **244196-49-4P**, 2-[3-(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]piperidine hydrogen oxalate **244196-50-7P**, 2-[3-(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-1-piperidineacetic acid ethyl ester **244196-51-8P**, 2-[3-(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-1-piperidineacetic acid ethyl ester hydrogen oxalate **244196-52-9P**, 4-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)carbonyl]-1-benzylpiperidine **244196-54-1P**, 4-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-1-benzylpiperidine hydrogen oxalate **244196-55-2P**, 4-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-1-piperidinepropionic acid ethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of dibenzazepines and analogs for treatment of painful and inflammatory conditions)

RN 13564-24-4 CAPLUS

CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-(3-piperidinylmethyl)- (9CI) (CA INDEX NAME)



RN 13564-30-2 CAPLUS
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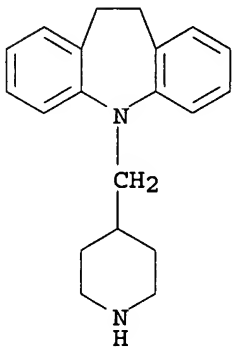

RN 244196-38-1 CAPLUS
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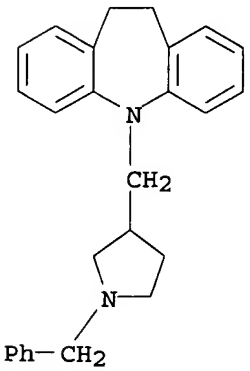

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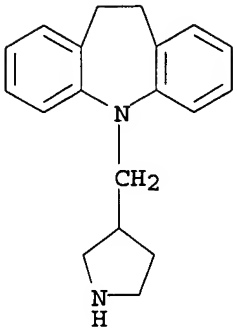
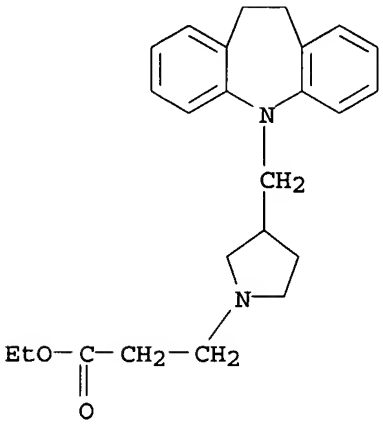


RN 244196-40-5 CAPLUS
CN 1-Pyrrolidinepropanoic acid, 3-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 244196-41-6 CAPLUS
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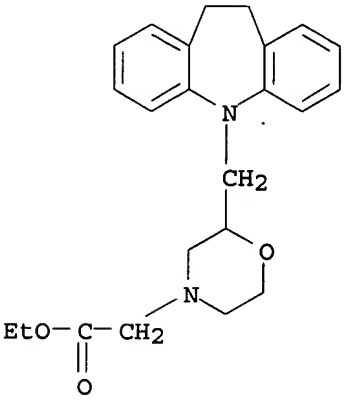

RN 244196-43-8 CAPLUS
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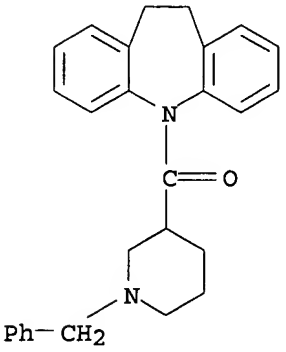

CM 2

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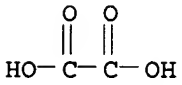

RN 244196-44-9 CAPLUS
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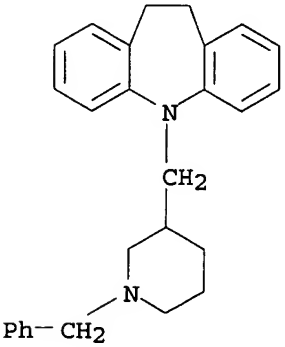

RN 244196-45-0 CAPLUS
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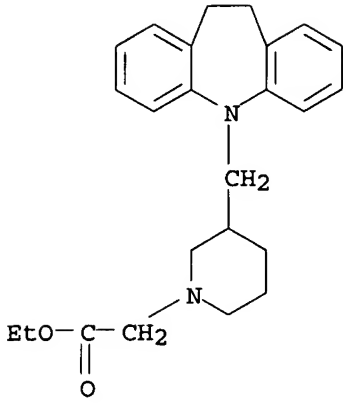
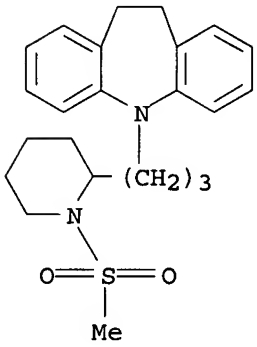
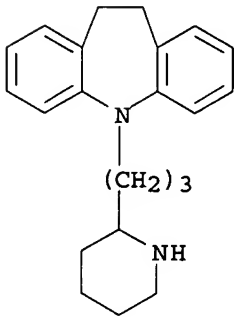


RN 244196-47-2 CAPLUS
CN Piperidine, 2-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)



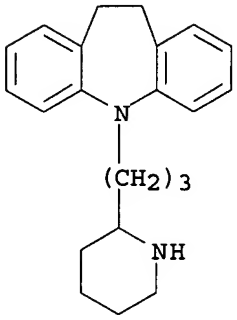
RN 244196-48-3 CAPLUS
CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[3-(2-piperidinyl)propyl]- (9CI) (CA INDEX NAME)



RN 244196-49-4 CAPLUS
CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[3-(2-piperidinyl)propyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

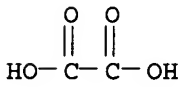
CM 1

CRN 244196-48-3
CMF C22 H28 N2

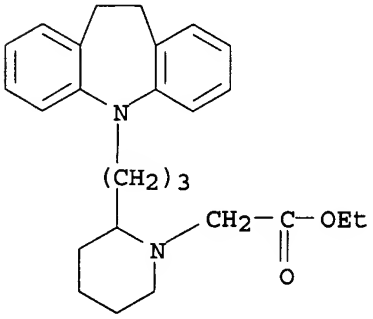


CM 2

CRN 144-62-7
CMF C2 H2 O4



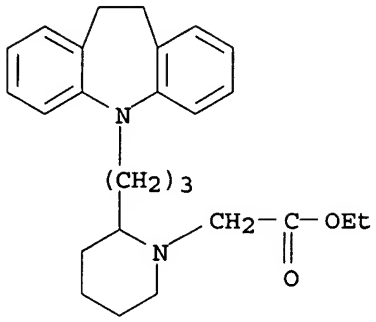
RN 244196-50-7 CAPLUS
CN 1-Piperidineacetic acid, 2-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 244196-51-8 CAPLUS
CN 1-Piperidineacetic acid, 2-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, ethyl ester, ethanedioate (1:1) (9CI) (CA INDEX NAME)

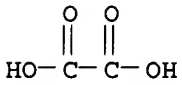
CM 1

CRN 244196-50-7
CMF C26 H34 N2 O2

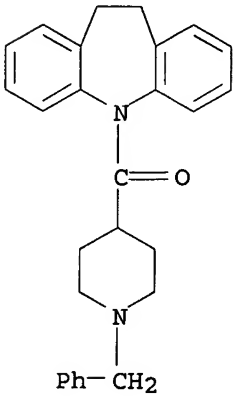


CM 2

CRN 144-62-7
CMF C2 H2 O4



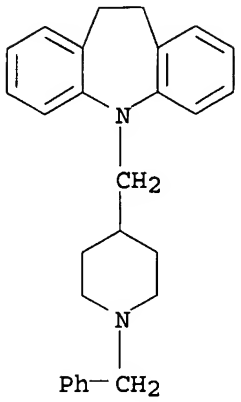
RN 244196-52-9 CAPLUS
CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[[1-(phenylmethyl)-4-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)



RN 244196-54-1 CAPLUS
CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

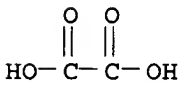
CM 1

CRN 244196-53-0
CMF C27 H30 N2

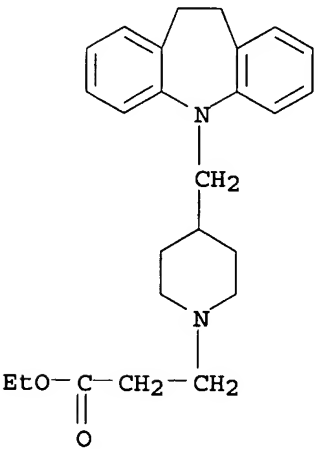


CM 2

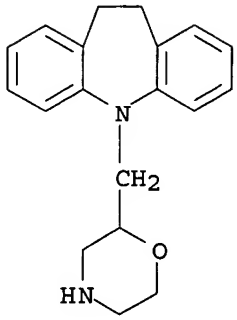
CRN 144-62-7
CMF C2 H2 O4



RN 244196-55-2 CAPLUS
CN 1-Piperidinepropanoic acid, 4-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-, ethyl ester (9CI) (CA INDEX NAME)



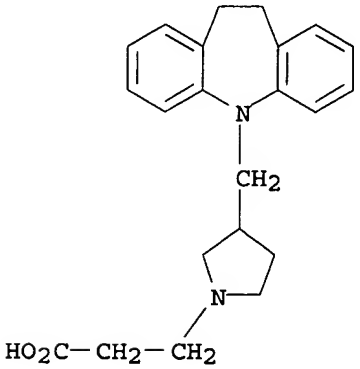
IT **61282-26-6**, 5-(2-Morpholinylmethyl)-10,11-dihydro-5H-dibenzo[b,f]azepine
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; prepn. of dibenzazepines and analogs for treatment of painful and inflammatory conditions)
RN 61282-26-6 CAPLUS
CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-(2-morpholinylmethyl)- (9CI) (CA INDEX NAME)



IT **244196-27-8P**, 3-[3-[(10,11-Dihydro-5H-dibenzo[b,f]azepin-5-yl)methyl]pyrrolidin-1-yl]**propionic** acid hydrochloride **244196-28-9P**, 2-[2-[(10,11-Dihydro-5H-dibenzo[b,f]azepin-5-yl)methyl]morpholin-4-yl]acetic acid **244196-29-0P**, 2-[2-[(10,11-Dihydro-5H-dibenzo[b,f]azepin-5-yl)methyl]morpholin-4-yl]acetic acid hydrogen oxalate **244196-30-3P**, 2-[2-[(10,11-Dihydro-5H-dibenzo[b,f]azepin-5-yl)methyl]morpholin-4-yl]acetic acid hydrochloride **244196-31-4P**, [3-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-1-piperidyl]acetic acid **244196-32-5P**, [3-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-1-piperidyl]acetic acid acetate **244196-33-6P**, 2-[3-(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-1-piperidineacetic acid hydrochloride **244196-34-7P**, 4-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-1-piperidinepropionic acid **244196-35-8P**, 4-[(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-1-piperidinepropionic acid hydrogen oxalate **244196-36-9P**, 3-[3-[(10,11-Dihydro-5H-dibenzo[b,f]azepin-5-yl)methyl]pyrrolidin-1-yl]**propionic** acid **244196-37-0P**, 2-[3-(10,11-Dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-1-piperidine]acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of dibenzazepines and analogs for treatment of painful and inflammatory conditions)

RN 244196-27-8 CAPLUS

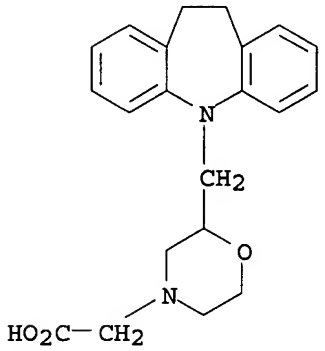
CN 1-Pyrrolidinepropanoic acid, 3-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



HCl

RN 244196-28-9 CAPLUS

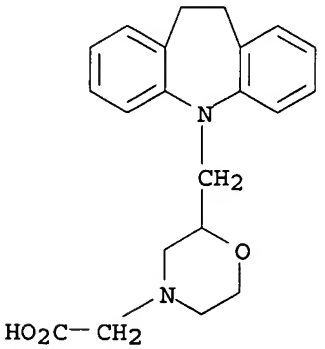
CN 4-Morpholineacetic acid, 2-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]- (9CI) (CA INDEX NAME)



RN 244196-29-0 CAPLUS
CN 4-Morpholineacetic acid, 2-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

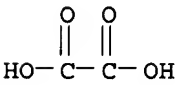
CM 1

CRN 244196-28-9
CMF C21 H24 N2 O3

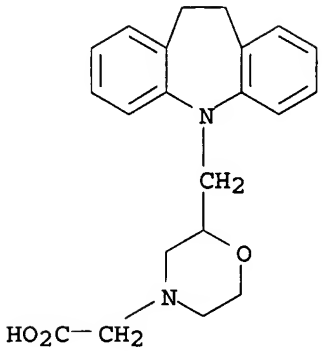


CM 2

CRN 144-62-7
CMF C2 H2 O4

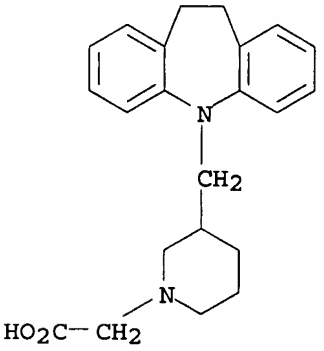


RN 244196-30-3 CAPLUS
CN 4-Morpholineacetic acid, 2-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

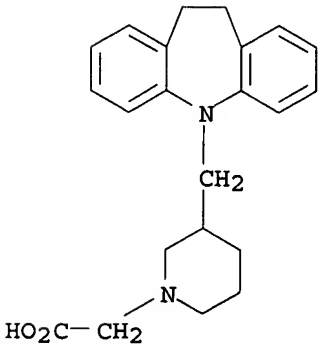
RN 244196-31-4 CAPLUS
CN 1-Piperidineacetic acid, 3-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]- (9CI) (CA INDEX NAME)



RN 244196-32-5 CAPLUS
CN 1-Piperidineacetic acid, 3-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-, monoacetate (9CI) (CA INDEX NAME)

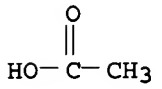
CM 1

CRN 244196-31-4
CMF C22 H26 N2 O2

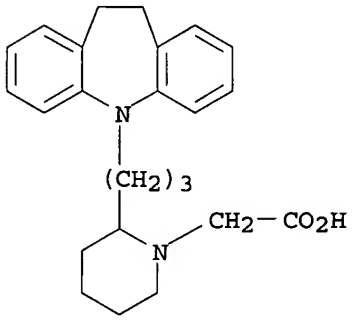


CM 2

CRN 64-19-7
CMF C2 H4 O2

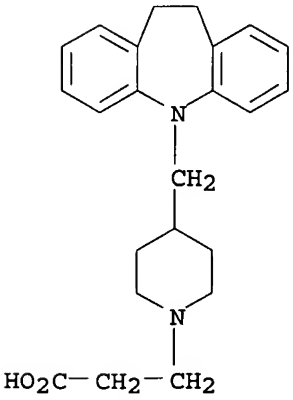


RN 244196-33-6 CAPLUS
CN 1-Piperidineacetic acid, 2-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 244196-34-7 CAPLUS
CN 1-Piperidinepropanoic acid, 4-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]- (9CI) (CA INDEX NAME)

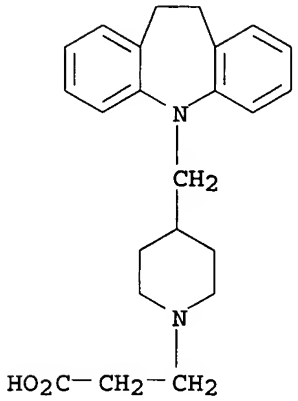


RN 244196-35-8 CAPLUS
CN 1-Piperidinepropanoic acid, 4-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

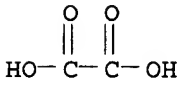
CRN 244196-34-7

CMF C23 H28 N2 O2

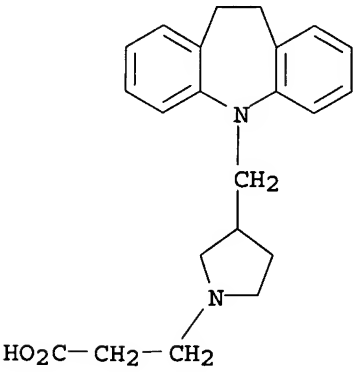


CM 2

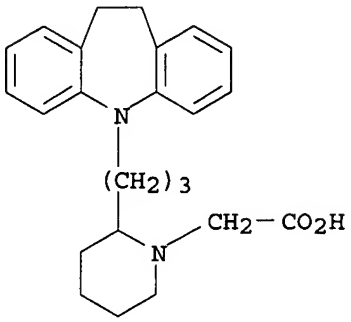
CRN 144-62-7
CMF C2 H2 O4



RN 244196-36-9 CAPLUS
CN 1-Pyrrolidinepropanoic acid, 3-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)methyl]- (9CI) (CA INDEX NAME)



RN 244196-37-0 CAPLUS
CN 1-Piperidineacetic acid, 2-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:34896 CAPLUS
DOCUMENT NUMBER: 130:110162
TITLE: Preparation of N-substituted azaheterocyclic compounds for the clinical treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiological role
INVENTOR(S): Andersen, Knud Erik; Jorgensen, Tine Krogh; Hohlweg, Rolf; Fischer, Erik; Olsen, Uffe Bang; Polivka, Zdenek; Sindelar, Karel; Valenta, Vladimir
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9900367	A1	19990107	WO 1998-DK273	19980622
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6040318	A	20000321	US 1998-98579	19980617
AU 9879074	A1	19990119	AU 1998-79074	19980622
EP 991621	A1	20000412	EP 1998-929235	19980622
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002515914	T2	20020528	JP 1999-505222	19980622
ZA 9805448	A	19990119	ZA 1998-5448	19980623
US 6066632	A	20000523	US 1999-376735	19990817
US 6100253	A	20000808	US 1999-376734	19990817
US 6114354	A	20000905	US 1999-375745	19990817

PRIORITY APPLN. INFO.:

DK 1997-751	A	19970625	
US 1997-51833P	P	19970707	
US 1998-98579	A3	19980617	
WO 1998-DK273	W	19980622	

OTHER SOURCE(S): MARPAT 130:110162
GI

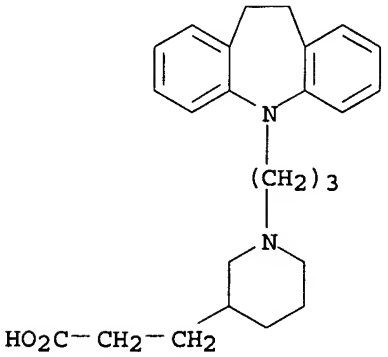
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1, R2 = H, halo, CF3, etc.; Y = >N-CH2-, >CH-CH2-, >C:CH- (only the first atom participates in the ring system); X = o-phenylene, O, S, etc.; r = 1-3; Z = II-V (wherein R3 = (CH2)pCO2H; p = 2-6)] and their salts, useful for the clin. treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role by eliciting neurogenic pain or inflammation as well as their use for treatment of indications caused by or related to the secretion and circulation of insulin antagonizing peptides, e.g. non-insulin-dependent diabetes mellitus (NIDDM) and ageing-assocd. obesity, were prepd. and formulated. Thus, reaction of 5-(3-bromo-1-propylidene)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene with 3-(piperidin-3-yl)**propionic** acid Et ester (prepn. given) in the presence of K2CO3 in DMF followed by hydrolysis of the resulting ester afforded VI.HCl which showed 42% inhibition of histamine induced hyperglycemia at 1.0 mg/kg.

IT **219608-69-2P 219608-74-9P 219608-88-5P**
219608-91-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-substituted azaheterocyclic compds. for the clin. treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role)

RN 219608-69-2 CAPLUS

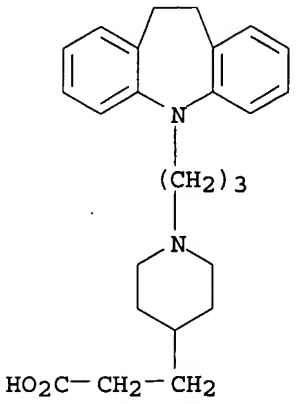
CN 3-Piperidinepropanoic acid, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

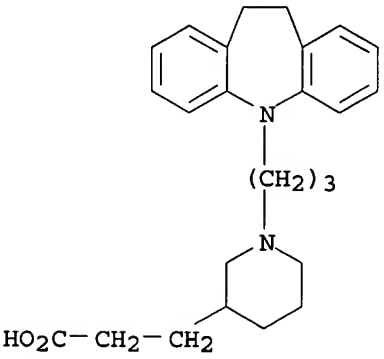
RN 219608-74-9 CAPLUS

CN 4-Piperidinepropanoic acid, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

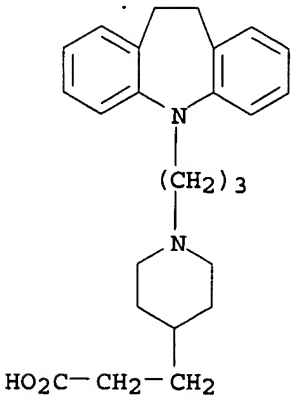


● HCl

RN 219608-88-5 CAPLUS
CN 3-Piperidinepropanoic acid, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]- (9CI) (CA INDEX NAME)



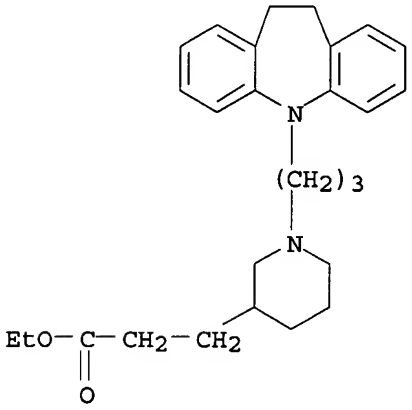
RN 219608-91-0 CAPLUS
CN 4-Piperidinepropanoic acid, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]- (9CI) (CA INDEX NAME)



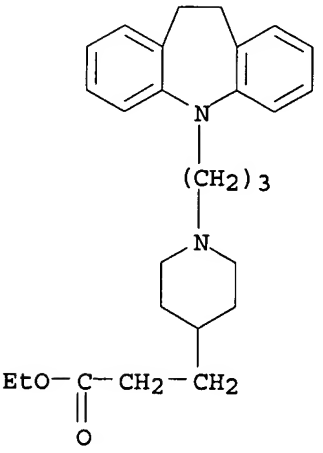
IT **219608-97-6P 219609-00-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-substituted azaheterocyclic compds. for the clin. treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role)

RN 219608-97-6 CAPLUS
CN 3-Piperidinepropanoic acid, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 219609-00-4 CAPLUS
CN 4-Piperidinepropanoic acid, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:28656 CAPLUS
DOCUMENT NUMBER: 128:102008
TITLE: Preparation and formulation of pyridine derivatives as antitumor agents and immunosuppressants
INVENTOR(S): Biedermann, Elfi; Hasmann, Max; Loser, Roland; Rattel, Benno; Reiter, Friedemann; Schein, Barbara; Seibel, Klaus; Vogt, Klaus
PATENT ASSIGNEE(S): Klinge Pharma G.m.b.H., Germany; Biedermann, Elfi; Hasmann, Max; Loser, Roland; Rattel, Benno; Reiter,

Friedemann; Schein, Barbara; Seibel, Klaus; Vogt, Klaus

SOURCE: PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9748397	A1	19971224	WO 1997-EP3244	19970620
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19624668	A1	19980219	DE 1996-19624668	19960620
ZA 9705443	A	19980210	ZA 1997-5443	19970619
AU 9732624	A1	19980107	AU 1997-32624	19970620
EP 912176	A1	19990506	EP 1997-928260	19970620
EP 912176	B1	20020925		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000512652	T2	20000926	JP 1998-502317	19970620
AT 224713	E	20021015	AT 1997-928260	19970620
ES 2181006	T3	20030216	ES 1997-928260	19970620
US 6451816	B1	20020917	US 1998-216482	19981218

PRIORITY APPLN. INFO.: DE 1996-19624668 A 19960620
WO 1997-EP3244 W 19970620
OTHER SOURCE(S): MARPAT 128:102008
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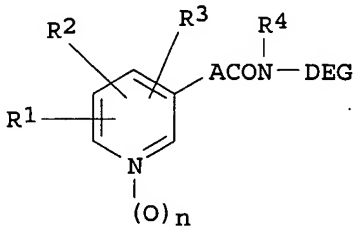

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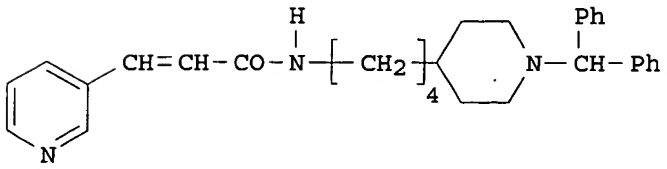
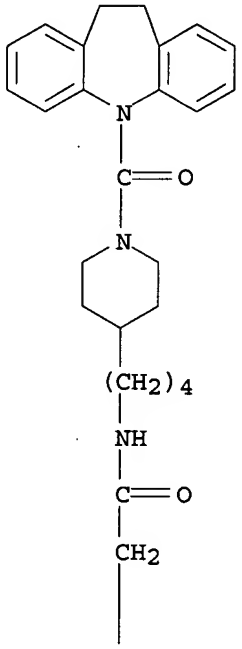


II

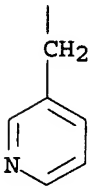
AB The title compd. I [R1 = H, halo, cyano, etc.; R2 = H, halo, hydroxy, alkyl, etc.; R3 = H, halo, alkyl, etc.; R4 = H, hydroxy, benzyloxy, etc.; n = 0 or 1; A = alkylene, etc.; D = alkylene, etc.; E = piperidine ring (generic structure given), etc.; G = H, etc.] are prepd. The title compd. II in vitro showed IC50 of 0.008 .mu.M against the WERI-Rb-1 retinoblastoma cells.

IT **200868-28-6P 201159-69-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyridine derivs. as antitumor agents and immunosuppressants)
RN 200868-28-6 CAPLUS
CN 3-Pyridinepropanamide, N-[4-[1-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)carbonyl]-4-piperidinyl]butyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

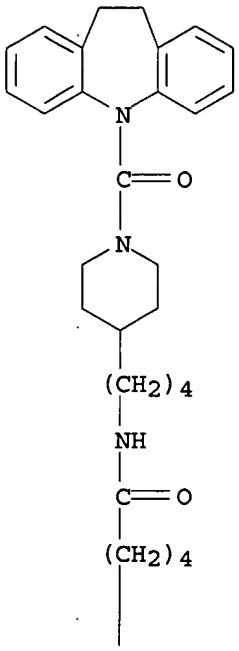


PAGE 2-A

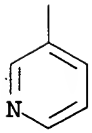


RN 201159-69-5 CAPLUS
CN 3-Pyridinepentanamide, N-[4-[1-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)carbonyl]-4-piperidinyl]butyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

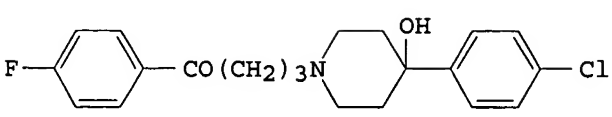


PAGE 2-A



L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1988:1685 CAPLUS
DOCUMENT NUMBER: 108:1685
TITLE: A rapid and simplified extraction of haloperidol from plasma or serum with Bond Elut C18 cartridge for analysis by high performance liquid chromatography
AUTHOR(S): Hayakari, Makoto; Hashimoto, Yumiko; Kita, Takeshi; Murakami, Satoshi
CORPORATE SOURCE: Sch. Med., Hirosaki Univ., Hirosaki, 036, Japan
SOURCE: Forensic Science International (1987), 35(1), 73-81
CODEN: FSINDR; ISSN: 0379-0738
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

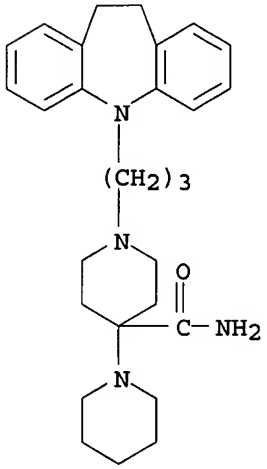
09/ 076,574

AB A method for the detn. of haloperiodol (HAL) (I) in plasma is based on HPLC with a reversed-phase column, ODS-C18. HAL is rapidly extd. from human plasma by using a Bond Elut C18 cartridge and its recovery is >90%. The mobile phase is a mixt. of 1% acetate/MeCN/tetrahydrofuran/triethylamine (69.5:28.2:1.9:0.4, by vol.). The method is rapid, simple, and free from interferences and gives good precision.

IT **5942-95-0**, Carpipramine **47739-98-0**
RL: ANT (Analyte); ANST (Analytical study)
(HPLC of)

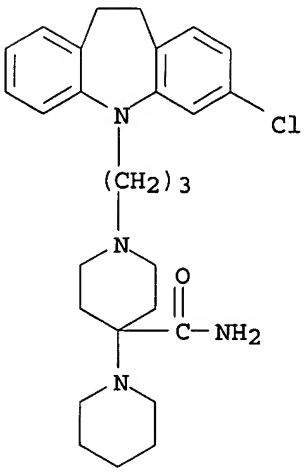
RN 5942-95-0 CAPLUS

CN [1,4'-Bipiperidine]-4'-carboxamide, 1'-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 47739-98-0 CAPLUS

CN [1,4'-Bipiperidine]-4'-carboxamide, 1'-[3-(3-chloro-10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1970:43496 CAPLUS

DOCUMENT NUMBER: 72:43496

TITLE: Substituted 5H-dibenz[b,f]azepines

INVENTOR(S): Fitzi, Konrad; Sallmann, Alfred

09/ 076,574

PATENT ASSIGNEE(S): Geigy, J. R., A.-G.
SOURCE: Ger. Offen., 79 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1910291	A	19691106	DE 1969-1910291	19690228
CH 501635	A	19710115	CH 1968-501635	19680229
NL 6902779	A	19690902	NL 1969-2779	19690221
DK 122725	B	19720404	DK 1969-982	19690221
US 3624075	A	19711130	US 1969-801801	19690224
FR 2002897	A5	19691031	FR 1969-5170	19690227
BE 729209	A	19690828	BE 1969-729209	19690228
AT 286994	B	19710111	AT 1969-2038	19690228
AT 286997	B	19710111	AT 1970-2017	19690228
AT 286996	B	19710111	AT 1970-2014	19690228
ES 364635	A1	19710201	ES 1969-364635	19690228
ES 364633	A1	19710201	ES 1969-364633	19690228
ES 364637	A1	19710201	ES 1969-364637	19690228
ES 364634	A1	19710201	ES 1969-364634	19690228
ES 364632	A1	19710201	ES 1969-364632	19690228
AT 287729	B	19710210	AT 1970-2015	19690228
AT 289815	B	19710510	AT 1970-2016	19690228
GB 1259648	A	19720105	GB 1969-1259648	19690228
BR 6906750	A0	19730419	BR 1969-206750	19690228
JP 49027876	B4	19740722	JP 1969-14996	19690228
JP 49029197	B4	19740801	JP 1971-48717	19710702

PRIORITY APPLN. INFO.: CH 1968-3055 19680229

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) have antiinflammatory, antiphlogistic, analgetic, a ntipyretic and uv absorbing properties and are prepd. by various known met hods. Thus, a mixt. of 16.5 g 5-acetyl-10,11-dihydro-5H-dibenz[b,f]azepine-3-carboxylic acid, 15 g KOH and 300 ml anhyd. EtOH is refluxed 16 hr to yield 10,11-dihydro-5H-dibenz[b,f]azepine-3-carboxylic acid (II), m. 1 96-7.degree. (EtOH). To a mixt. of 70 ml Ac2O and 35 ml HCO2H, kept 1 hr at 35-40.degree. is added with stirring 11 g II in 1.5 hr at 45-50.degree. and the mixt. is stirred 2.5 hr at 45-50.degree. and 8 hr at 20-5.degree. to yield 5-formyl-10,11-dihydro-5H-dibenz[b,f]azepine-3-carboxylic acid (III), m. 226-8.degree. (EtOH). To a mixt. of 9.2 g 5-butyryl-10,11-dihydro-5H-dibenz[b,f]azepine, 3.43 g AcCl and 50 ml CS2 is added in 40 min at 40.degree. portionwise 19 g anhyd. AlCl3, and the mixt. is refluxed 1 hr. To the mixt. is added 3.43 g AcCl and the mixt. is refluxed 15 hr. To this mixt. is added 50 ml CS2, 1.5 g AcCl, and 5 g anhyd. AlCl3 and refluxing is continued 20 hr to yield oily 3-acetyl-5-butyryl-10,11-dihydro-5H-dibenz[b,f]azepine (IV). To a soln. of 30.7 g IV in 300 ml dioxane and 100 ml H2O with stirring in 30 min at 0.degree. is added dropwise 240 ml 11% aq. NaOCl soln. and stirring is continued 30 min at 0.degree. and 2 hr at room temp. to yield 5-butyryl-10,11-dihydro-5H-dibenz[b,f]-azepine-3-carboxylic acid, m. 108-10.degree. (C6H6-cyclohexane). Diborane, prepd. from 7 g NaBH4, 38.8 ml BF3-etherate and 230 ml diethylene glycol dimethyl ether is added with stirring in 1.5 hr at 8-12.degree. to a soln. of 9.5 g III in 100 ml freshly distd. anhyd. tetrahydrofuran (THF) and the mixt. is stirred 2 hr at 0-5.degree. and worked up to yield oily 5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine-3-methanol (V). Similarly is prepd. the oily 5-butyl analog of V. A soln. of 8.5 g V in 300 ml CHCl3 is satd. at 0.degree. with HBr, and stirred 12 hr at 20-5.degree. to yield oily 3-bromomethyl-5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine (VI). Similarly is prepd. the oily 5-butyl analog of VI. A mixt. of 12.7 g VI,

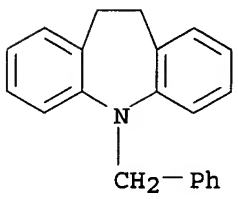
6.3 g KCN, and 100 ml dimethyl sulfoxide (DMSO) is stirred 5 hr at 40-50.degree. to yield 5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine-3-acetonitrile (VII), m. 78-81.degree. (EtOAc). Similarly is prepd. the oily 5-butyl analog of VII. A soln. of 10 g VII in 500 ml CHCl3 and 50 ml anhyd. EtOH is satd. at 0-5.degree. with HCl and the mixt. is stirred 14 hr at 20-5.degree. and evapd. The residue is stirred 5 hr at 40.degree. with 100 ml dioxane and 20 ml H2O and evapd. The crude Et ester is refluxed 1 hr with 100 ml EtOH and 30 ml 5N aq. NaOH to yield 5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine-3-acetic acid (VIII), m. 140-1.degree. (cyclohexane). Similarly is prepd. the oily 5-butyl analog (IX) of VIII. Similarly, starting with 3-acetyl-10,11-dihydro-5H-dibenz[b,f]azepine (iXa) the following I are prepd. (R1 = R4 = H) (R2, R3, and phys. co nsts. given): Ac, CHO, m. 111-13.degree. (C6H6-petroleum ether); CHMe(OH), Me, oil; CHMeBr, Me, oil; CHMeCN, Me, oil; CHMeCO2H, Me (X), m. 138-40.degree. (C6H6). To 120 ml dimethylformamide (DMF) is added dropwise with stirring in 10 min at 10.degree. 61 g distd. POCl3. To this mixt., cooled to 0.degree. is added dropwise with stirring in 1 hr <10.degree. a soln. of 38 g 5-benzyl-10,11-dihydro-5H-dibenz[b,f]azepine, b0.15 178-8 1.degree., m. 66-8.degree. (EtOH) (prepd. from 10,11-dihydro-5H-dibenz[b,f]azepine (XI) and PhCH2Cl with NaNH2 in boiling PhMe) in 60 ml DMF and the mixt. is stirred 1 hr at 70-5.degree. to yield 5-benzyl-10,11-dihydro-5H-dibenz[b,f]azepine-2-carboxaldehyde (XII), m. 99.5-101.degree. (cyclohexane). To a mixt. of 11.7 g LiAlH4 and 250 ml anhyd. Et2O, cooled <5.degree. is added under N dropwise with stirring under ice-cooling a soln. of 50 g XII in 600 ml dry Et2O and 150 ml dry THF and the mixt. is stirred 18 hr at room temp. to yield 5-benzyl-10,11-dihydro-5H-dibenz[b,f]-azepine-2-methanol (XIII), b0.01 190-200.degree., which is converted with HBr in CHCl3 at -5.degree. into oily 2-bromomethyl-5-benzyl-10,11-dihydro-5H-dibenz[b,f]azepine (XIV). A soln. of 1.6 g XIII in 20 ml dry Et2O and 2 ml dry C5H5N is added dropwise with stirring to a cooled (0.degree.) soln. of 2 ml SOCl2 and 2 ml pentane and the mixt. is stirred 1 hr at 0.degree. to yield oily 2-chloromethyl-5-benzyl-10,11-dihydro-5H-dibenz[b,f]azepine (XV). Both XIV and XV are converted with NaCN in DMSO into 5-benzyl-10,11-dihydro-5H-dibenz[b,f]azepine-2-acetonitrile, m. 96-8.degree. (Et2O), which is converted (as with VIII) into 10,11-dihydro-5H-dibenz-[b,f]azepine-2-acetic acid (XVI), m. 155-8.degree. (Et2O). Starting with XI, which is converted with MeI and NaH in DMF at 70.degree. into 5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine, m. 106-7.degree. (EtOH), are prepd. the following I (R2 = R4 = H, R3 = Me) (R1 and phys. consts. given): CHO, m. 90-3.degree. (EtOAc-Et2O); CH2OH, m. 78-9.degree. (Et2O-petroleum ether); CH2Cl, oil; CH2CN, m. 70-1.degree. (Et2O-petroleum ether); CH2CO2H, m. 121-3.degree.; CH2CO2Na, m. 192-4.degree. (EtOAc). Similarly, starting with 3-chloro-10,11-dihydro-5H-dibenz[b,f]azepine are prepd. the following I (R3 = Me) (R1, R2, R4, and phys. consts. given): H, Cl, H, b0.001 170.degree., m. 56-8.degree. (EtOH); mixt. of CHO, H, Cl, and CHO, Cl, H, oil; CH2OH, H, Cl, oil (sepn. of the 3-Cl isomer is given); CH2Cl, H, Cl, oil; CH2CN, H, Cl, m. 117-19.degree. (MeOH); CH2CO2H, H, Cl (XVIa), m. 175-87.degree. (EtOAc-petroleum ether). A mixt. of 1.2 g Me 10,11-dihydro-5H-dibenz[b,f]azepine-2-acetate, 100 ml EtOH, and 15 ml 2N aq. NaOH is refluxed 30 min to yield XVI. A mixt. of 2 g 10,11-dihydro-5H-dibenz-[b,f]azepine 3-acetic acid (XVII), 50 ml anhyd. MeOH and 200 mg .rho.-toluenesulfonic acid is refluxed 14 hr to yield the oily Me ester of XVII, which is converted by methods already described into the following I (R1 = R4 = H) (R2, R3 and phys. consts. given): CH2CO2Me, CHO, 85-7.degree. (Et2O); CH2CO2H , CHO, 182-4.degree. (MeOH-EtOAc); CH2CO2Me, Me, oil; VIII. Similarly are prepd. the following I (R1 = R4 = H) (R2, R3 and phys. consts. given): CMeHCO2Me, H, -; CMeHCO2Me, CHO, oil CMeHCO2Me, Me, -; X; CH2CO2Me, Bu, oil; IX. A mixt. of 13 g IXa, 60 ml MeOH and 28 ml MeI is heated 24 hr at 100.degree. in a closed vessel to yield oily 3-acetyl-5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine (XVIII). A mixt. of 24 g XVIII, 5 g S and 50 ml morpholine is refluxed 18 hr to yield 4-(5-methyl-10,11-dihydro-5H-

dibenz[b,f]azepine-3-thioacetyl)morpholine, which is refluxed 4.5 hr with a mixt. of 15 g KOH and 250 ml anhyd. ethylene glycol to yield VIII. Similarly, starting with 3,5-diacetyl-10,11-dihydro-5H-dibenz[b,f]azepine is prepd. 10,11-dihydro-5H-dibenz[b,f]azepine-3-acetic acid, m. 133-5.degree. (C6H6). To a soln. of 300 g 3-chloro-10,11-dihydro-5H-dibenz[b,f]azepine in 1000 ml dry C6H6 is added dropwise at 60-70.degree. a soln. of 125 g AcCl in 600 m l C6H6 and the mixt. is refluxed 5 hr to yield 3-chloro-5-acetyl-10,11-dihydro-5H-dibenz[b,f]azepine (XIX), m 119-20.degree. (EtOH). To a mixt. of 163.5 g XIX, 850 ml CS2 and some iodine at 40.degree. is added 135 g AcCl; 250 g anhyd. AlCl3 is added in 1 hr and the mixt. is refluxed 1 hr. To the mixt. is added 125 g AlCl3, and the mixt. is refluxed 12 hr, followed by addn. of 66.6 g AlCl3 and 26.1 g AcCl and refluxing is continued 24 hr. This process is repeated 6 times to yield, after 1 week, oily 3,5-diacetyl-7-chloro-10,11-dihydro-5H-dibenz[b,f]azepine, which is converted into 7-chloro-10,11-dihydro-5H-dibenz[b,f]-azepine-3-acetic acid (XIXa), m. 155-7.degree. (C6H6). A soln. of 23.7 g 5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine-2-carboxaldehyde, m. 90-3.degree., 17.5 g NH2OH.HCl, 18 ml C5H5N and 200 ml EtOH is refluxed 1 hr to yield 5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine-2-carboxaldoxime (XX), m. 148-50.degree. (Et2O-petroleum ether). A mixt. of 30.3 g XX and 180 ml Ac2O is refluxed 2 hr to yield 2-cyano-5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine (XXI), m. 120-2.degree. (EtOH). To a Grignard soln., prepd. from 6 g Mg, 3.5 g MeI, 200 ml Et2O and 70 ml C6H6 is added a soln. of 23.4 g XXI in 150 ml Et2O, and the m ixt. is refluxed 5 hr and worked up to yield 2-acetyl-5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine, m. 80-3.degree. (Et2O-petroleum ether), which is converted into 5-methyl-10,11-dihydro-5H-dibenz-[b,f]azepine-2-acetic acid (XXII), m. 121-3.degree. (Et2O-petroleum ether). To a soln. of 5 g 5-methyl-10,11-dihydro-5H-dibenz-[b,f]azepine-2-acetonitrile (XXIII), m. 70-1.degree., in 50 ml Me2CO and 10 ml H2O at 20.degree. is added 6 ml 30% aq H2O2, followed by 2 ml 2N aq. NaOH and the mixt. i s heated 20 min at 50.degree.. To the mixt. is added 6 ml 30% aq. H2O2 and 2 ml 2N aq. NaOH and the mixt. is heated 4 hr at 50.degree. to yield 5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine-2-acetamide (XXIV), m. 140-2.degree. (MeOH). A mixt. of 2 g XXIV, 9 g KOH, and 60 ml BuOH is refluxed 1 hr to yield XXII. A mixt. of 16 g XXIII, 75 g KOH, and 500 ml BuOH is refluxed 2 hr to yield XXII. Similarly, starting with 7-chloro-5-methyl-10,11-dihydro-5H-dibenz[b,f]a zepine-2-acetonitrile, m. 117-19.degree., is prepd. XVIa; and VII is conv erted with KOH in ethylene glycol into VIII. A soln. of 32 g XXII in 120 ml N aq. NaOH is evapd. at 50.degree./11 mm. followed by evapn. with 100 ml C6H6. To the residue in 350 ml DMF at 40.degree. is added 18.5 g Et2SO4. After 15 min 5 g Et2SO4 is added and the mixt. is stirred 30 min at 40.degree. to yield the Et ester (XXV) of XXII, b0.001 170.degree.. To a mixt. of 2.5 g NaH in paraffin (1:1) and 80 ml hexamethylphosphoric acid triamide (XXVI) is added at 40.degree. under N a soln. of 14.8 g XXV in 50 ml XXVI. The mixt. is stirred 45 min at 50.degree., after cooling to 30.degree. 7.8 g. EtI is a dded dropwise and the mixt. is stirred 10 hr at 60.degree. to yield 5-methyl-10 ,11-dihydro-5H-dibenz[b,f]azepine-2-butyric acid (Et ?) ester, which is sapond. with aq. alc. NaOH to yield 5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine-2-butyric acid, m. 108-13.degree. (Et2O-petroleum ether). Starting with 3,5-diacetyl-10,11-dihydro-5H-dibenz[b,f]azepine (XXVII) which is converted with NaOCl in dioxane into 5-acetyl-10,11-dihydro-5H-dibenz[b,f]azepine-3-carboxylic acid (XXVIII), m. 197-8.degree. (Me2CO), is prepd. with MeOH and .rho.-toluenesulfonic acid the Me ester of XXVIII, m. 122-4.degree., which is reduced with LiAlH4 in THF at -70.degree. to yield 5-acetyl-10,11-dihydro-5H-dibenz[b,f]azepine-3-methanol (XXIX) m. 118-20.degree. (C6H6). To a soln. of 30 g XXIX in 300 ml CHCl3 is added with stirring at 0-5.degree. in 40 min a mixt. of 70 ml PBr3 and 100 ml CHCl3 and the mixt. is stirred 8 hr at 20-5.degree. to yield 3-bromomethyl-5-acetyl-10,11-dihydro-5H-di benz[b,f]azepine, m. 106-7.degree. (Et2O), which is converted with KCN in DMSO into 5-acetyl-10,11-dihydro-5H-dibenz[b,f]azepine-3-acetonitrile, m.

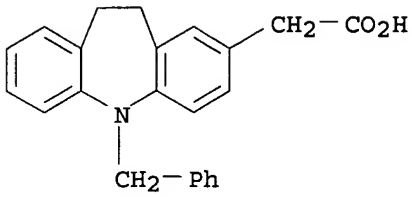
97-100.degree. (C6H6-petroleum ether), which is converted via 5-acetyl-10,11-dihydro-5H-dibenz[b,f]azepine-3-acetic acid, m. 163-5.degree. (EtOAc-petroleum ether), into 10,11-dihydro-5H-dibenz[b,f]azepine-3-acetic acid, m. 133-5.degree. (C6H6), which is also prepd. from 5-butyryl-10,11-dihydro-5H-dibenz[b,f]azepine-3-acetic acid. Starting with XXVII are prepd. the following I (R1 = R4 = H) (R2, R3, and phys. consts. given): CMeHOH, Ac, oil; CMeHOH, CHO, m. 111-13.degree.; CMeHBr, Ac, oil; CMeHCN, Ac, oil; CMeHCO2H, Ac, m. 153-4.degree.; CMeHCO2H, H, m. 129-31.degree.; and further the following I (R1 = H, R4 = Cl) (R2, R3, and phys. consts. given): CO2H, Ac, m. 264-6.degree. (Et2O-petroleum ether); CO2Me, Ac, m. 130-2.degree. (MeOH); CH2OH, Ac, -; CH2Br, Ac, -; CH2CN, Ac, m. 112-14.degree. (C6H6-petroleum ether); CH2CO2H, Ac, m. 128-9.degree. (C6H6); XIXa. A mixt. of 4 g 5-benzyl-10,11-dihydro-5H-dibenz[b,f]-azepine-2-acetonitrile, m. 96-8.degree., 6 g KOH and 40 ml BuOH is refluxed 7 hr to yield 5-benzyl-10,11-dihydro-5H-dibenz[b,f]-azepine-2-acetic acid (XXX), m. 138-9.degree. (Et2O). A mixt. of 1.37 g XXX and 40 ml MeOH is hydrogenated 15 min with 1 atm H at room temp. and 0.25 g 10% Pd/C as catalyst to yield XVI. A mixt. of 7 g XVII, 14 ml MeI and 70 ml CHCl3 is heated 24 hr at 100.degree. in a closed vessel to yield VIII and the Me ester of VIII. Similarly, XIXa is converted into 7-chloro-5-methyl-10,11-dihydro-5H -dibenz[b,f]azepine-3-acetic acid (XXXI) and the Me ester of XXXI , which is sapond. after purification to yield XXXI, m. 156-8.degree. (Et2O-petroleum ether). To a mixt. of 11.8 g XXV and 37 ml diethyl carbonate, heated to 80.degree. is added dropwise a soln. of 1.32 g Na in 60 ml anhyd. EtOH, and the mixt . is heated to 220.degree., and 30 ml diethyl carbonate is added and the mixt. is heated 0.5 hr at 220.degree. to yield 5-methyl-10,11-dihydro-5H-dibenz[b,f]azepine-2-malonic acid di Et ester (XXXII), b0.001 190-5.degree.. A soln. of 5.9 g XXXII in 15 ml anhyd. EtOH is added at 50.degree. to a soln. of 0.5 g Na in 80 ml EtOH and the mixt. is stirred 0.5 hr at 50.degree.. To this mixt. is added dropwise with stirring 3.5 g MeI and the mixt. is refluxed with stirring 4 hr. After addn. of 3.5 g MeI, refluxing is continued 2 hr to yield oily meth yl-(5-methyl-10,11-dihydro-5H-dibenz[b,f]azepin-2-yl)-malonic acid di E t ester (XXXIII). Similarly is prepd. oily ethyl-(5-methyl-10,11-dihydro-5H-dibenz[b,f]azepin-2-yl)-malonic acid di Et ester (XXXIV). A mixt. of 5.5 g XXXIII, 3.5 g KOH, 12 ml H2O, and 40 ml BuOH is refluxed 4 hr to yield 2-(5-methyl-10,11-dihydro-5H-dibenz[b,f]azepin-2-yl) **propionic** acid, m. 153-7.degree. (EtOAc). Similarly, starting with XXXIV is prepd. 2-(5-methyl-10,11-dihydro-5H-dibenz[b,f]azepin-2-yl)-butyric acid, m. 108-13.degree. (Et2O-petroleum ether).

IT **13080-72-3P 25953-43-9P 25960-90-1P 25960-94-5P 25960-97-8P 25960-98-9P 25961-01-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 13080-72-3 CAPLUS
CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 25953-43-9 CAPLUS
CN 5H-Dibenz[b,f]azepine-2-acetic acid, 5-benzyl-10,11-dihydro- (8CI) (CA INDEX NAME)



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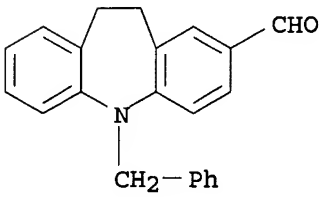

RN 25960-94-5 CAPLUS
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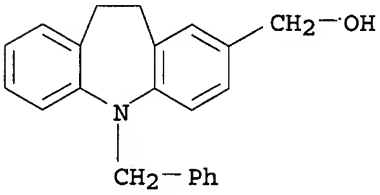

RN 25960-97-8 CAPLUS
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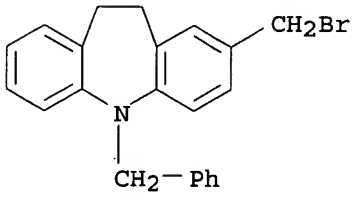

RN 25960-98-9 CAPLUS
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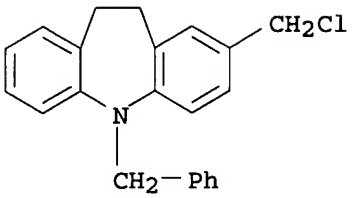
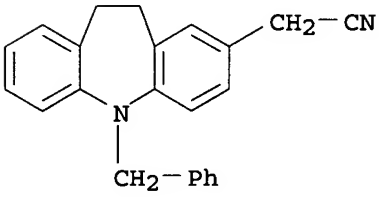


RN 25961-01-7 CAPLUS
CN 5H-Dibenz[b,f]azepine-2-acetonitrile, 10,11-dihydro-5-(phenylmethyl)-(9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1968:95776 CAPLUS
DOCUMENT NUMBER: 68:95776
TITLE: Phenothiazine derivatives. VII. Preparation of selectively acting phenothiazine derivatives
AUTHOR(S): Toldy, Lajos; Toth, Istvan; Borsy, Jozsef
CORPORATE SOURCE: Inst. Arzneimittelforsch., Budapest, Hung.
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CODEN: ACASA2; ISSN: 0001-5407
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LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB A no. of phenothiazines were prepd. that showed significant antiulcerogenic and coronary-enlargening activity and in certain cases selectively. The compds. tested are those listed in the table (Ia) and in the following 3 series. Series A, 3-substituted (R)-10-substituted(R')phenothiazines [R, R', no., and m.p. (deriv.) given]: H, PhCH2CHMeNH(CH2)3, XVIII, 185.degree. (oxalate); Cl, PhCH2CHMeNH(CH2)3, XIX, 159-60.degree. (hydrochloride); Cl, PhCH2CHMeNMe(CH2)3, XX, 175.degree. (oxalate); H, PhCH2CHMeNHCOCH2CH2, XXI, 121-3.degree.; Cl, PhCH2CHMeNHCOCH2CH2, XXII, 111-13.degree.. Series B, 5-substituted (R)-iminodibenzyls [R, no., and m.p. (deriv.) given]: o-xylyl, XXIII, 197-200.degree. (difumarate); 3-[4-(2-phenylisopropyl)-1-piperazinyl] propionyl, XXIV, 208-10.degree. (difumarate); 3-[4-(2-phenylisopropyl)-1-piperazinyl]ethyl, XXV, 252-4.degree. (dihydrochloride); PhCH2CHMeNH(CH2)3, XXVI, 188-91.degree. (oxalate); PhCH2CHMeNMeCH2CH2, XXVII, 173-5.degree. (oxalate). Series C, PhCH2CHMeR [R, no., and m.p. (deriv.) or b.p. given]: morpholino, XXVIII, b1 133.degree.; hexamethylenimino, XXIX, b0.5 120-30.degree.; heptamethylenimino, XXX, b0.8 165.degree.; 4-(benzyloxycarbonyl)-1-piperazinyl, XXXI, 153-5.degree. (fumarate); 4-(p-chlorobenzyloxycarbonyl)-1-piperazinyl, XXXII, 163-5.degree. (hydrochloride); 3,4,5-(MeO)3C6H2CONH, XXXIII, 164-6.degree.. Series C was pharmacol. uninteresting. III, VIII, and XX equaled and VI and XXVII exceeded the ulcer-arresting action of chloropromazine and chlorobenzoxamine, and the action of VI and XXVII was selective. Neither VI nor XXVII had anticholinergic activity. XIV showed strong, selective coronary-enlargening activity, while XV showed stronger

tranquilizing action than methophenazine and at the same time an intense coronary-enlargening action. [TABLE OMITTED] 3-Trifluoromethylphenothiazine (34.5 g.) and 8.5 g. NaNH2 in PhMe was refluxed 2 hrs., treated at 60.degree. with 14 ml. propylene oxide in PhMe dropwise during 2 hrs., refluxed 2 hrs., and treated with MeOH and then H2O to give 16 g. 3-trifluoromethyl-10-.beta.-hydroxypropylphenothiazine (XXXIV), b0.2 168-72.degree.. XXXIV (20.5 g.) and 10.3 ml. mesyl chloride in pyridine yielded 23 g. (crude) 3-trifluoromethyl-10-.beta.-mesyloxypropylphenothiazine (XXXV), m. 108-10.degree. (1:1 C6H6-Me2CO). XXXV (20 g.) and 20 g. N-.beta.-hydroxyethylpiperazine in 200 ml. xylene was refluxed 8 hrs. and cooled, the soln. decanted from oil and washed with H2O, the xylene soln. extd. with 15% tartaric acid soln., the ext. basified, and the washed and dried syrup treated with fumaric acid in hot dry EtOH to give 10 g. XIII difumarate (EtOH). Similarly were prepd. II, III, IV, VI, IX, X, XVII, XXIII, XXIV, XXVIII, XXIX, and XXX (sometimes in C6H6, PhMe, or morpholine). Treatment of XIII in ClCH2CH2Cl with 3,4,5-(MeO)3C6H2COCl gave XIV. VII, XV, and .beta.-(3-chloro-10-phenothiazinyl)**propionic** acid [2-methoxy-4-(diethylcarbamoyl)]phenyl ester (m. 119-21.degree.) were prepd. similarly. XI and XII were prepd. by esterification in pyridine, Treatment of 5 g. PhCH2Ac and 8.7 g. 5-(.gamma.-aminopropyl)iminodibenzyl in EtOH with H and 6 g. Raney Ni at 60.degree. and 25 atm. gave XXVI (5 g. as the oxalate). XVIII was prepd. similarly. 5-(.beta.-Hydroxyethyl)iminodibenzyl (13.4 g.) and 6.5 ml. mesyl chloride in CHCl3-pyridine at 0-25.degree. gave 12 g. 5-.beta.-mesyloxyethyliminodibenzyl (XXXVI), m. 130-2.degree.. XXXVI (6 g.) was shaken with 4.25 g. PhCH2CHMeNHMe and 5.3 ml. Et3N in EtOH 8 hrs. to give XXVII (1.2 g. as the oxalate). I, VIII (8 days shaking), XIX, XX, XVI, XXV, and 3-chloro-10-[.gamma.-[(1-methyl-4-diethylaminobutyl)amino]propyl]phenothiazine (di-maleate m. 174-8.degree.) were similarly prepd. Dropwise addn. of 4.68 g. .beta.-(10-phenothiazinyl)propionyl chloride in C6H6 to 2.18 g. PhCH2CHMeNH2 and 2 ml. Et3N in cold C6H6 and after 3 hrs. the mixt. refluxed 1 hr. gave 1.7 g. XXI. Similarly were prepd. XXII, XXXI, XXXII, and XXXIII. V was prepd. from 3-chloro-10-(chloroacetyl)phenothiazine and N-(o-xylyl)piperazine in Me2CO. 3-Trifluoromethyl-10-[.gamma.-[4-(.beta.-hydroxyethyl)-1-piperazinyl]propyl]phenothiazine, b0.2 240-4.degree., was prepd. from 3-trifluoromethylphenothiazine and 1-(.gamma.-chloropropyl)-4-(hydroxyethyl)piperazine. PhCH2COCH2NMe2 (35 g.) in 17% NH3EtOH with H and Raney Ni gave 7.2 g. PhCH2CH(NH2)CH2NMe2, b2 95-100.degree., and [Me2NCH2(PhCH2)CH]2NH, b2 142.degree..

IT **18455-20-4P 18455-21-5P 18484-09-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

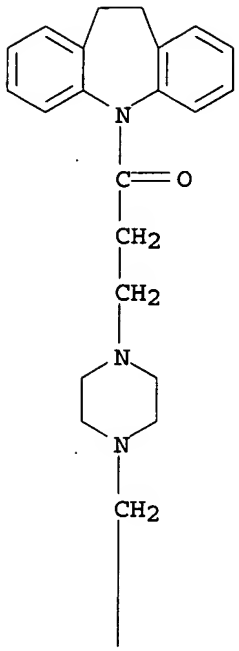
RN 18455-20-4 CAPLUS

CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[3-[4-(o-methylbenzyl)-1-piperazinyl]propionyl]-, fumarate (1:2) (8CI) (CA INDEX NAME)

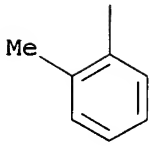
CM 1

CRN 47724-16-3
CMF C29 H33 N3 O

PAGE 1-A



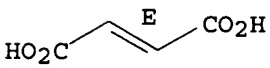
PAGE 2-A



CM 2

CRN 110-17-8
CMF C4 H4 O4

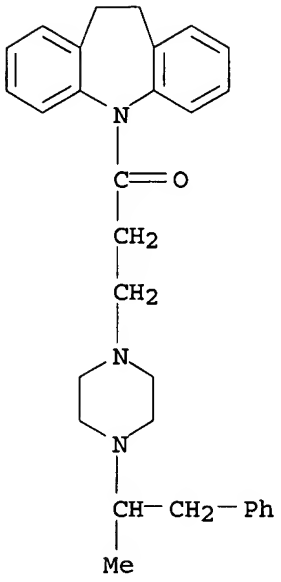
Double bond geometry as shown.



RN 18455-21-5 CAPLUS
CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[3-[4-(.alpha.-methylphenethyl)-1-piperazinyl]propionyl]-, fumarate (1:2) (8CI) (CA INDEX NAME)

CM 1

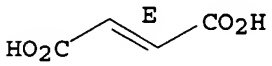
CRN 47742-46-1
CMF C30 H35 N3 O



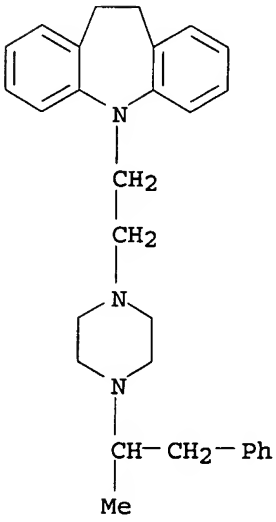
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 18484-09-8 CAPLUS
CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[2-[4-(.alpha.-methylphenethyl)-1-piperazinyl]ethyl]-, dihydrochloride (8CI) (CA INDEX NAME)



● 2 HCl

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1966:51966 CAPLUS

09/ 076,574

DOCUMENT NUMBER: 64:51966
ORIGINAL REFERENCE NO.: 64:9696d-g
TITLE: Dibenzazepines
PATENT ASSIGNEE(S): J. R. Geigy A.-G
SOURCE: 20 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 661191		19650916	BE	
FR 1434449			FR	
GB 1040740			GB	
NL 6503276			NL	

PRIORITY APPLN. INFO.: CH 19640316

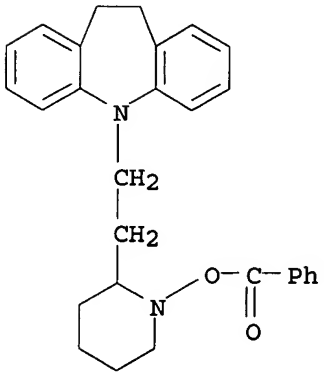
GI For diagram(s), see printed CA Issue.

AB Compds. of the formula I and II with antidepressant activity were prepd. Thus, a soln. of 30 g. 82% benzoyl peroxide in 70 cc. $CHCl_3$ was dried over Na_2SO_4, dild. with 130 cc. abs. Et_2O, a soln. of 27 g. 5-(3-methylamino propyl)-10,11-dihydro-5H-dibenz[b,f]azepine (III) in 200 cc. Et_2O added by stirring gradually within 1 hr. at 0-5.degree. the mixt. maintained at 20.degree. 2 to 4 hrs., cooled to 0.degree., the pptd. III filtered off and the filtrate evapd. to give I (X = CH_2CH_2, Y = H, A = $(CH_2)_3$, R1 = Me, R2 = Bz), m. 120-2.degree. (MeOH). Similarly, the tabulated I were prepd. Similarly, II (R2 = Bz), m. 132.degree., and II (R2 = H), m. 146-7.degree., were prepd.

IT **5227-89-4**, 5H-Dibenz[b,f]azepine, 5-[2-[1-(benzoyloxy)-2-piperidyl]ethyl]-10,11-dihydro- **5600-11-3**, 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[2-(1-hydroxy-2-piperidyl)-ethyl]- (prepn. of)

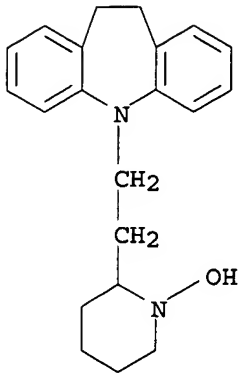
RN 5227-89-4 CAPLUS

CN 5H-Dibenz[b,f]azepine, 5-[2-[1-(benzoyloxy)-2-piperidyl]ethyl]-10,11-dihydro- (7CI, 8CI) (CA INDEX NAME)



RN 5600-11-3 CAPLUS

CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[2-(1-hydroxy-2-piperidyl)ethyl]-(7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1964:31000 CAPLUS
DOCUMENT NUMBER: 60:31000
ORIGINAL REFERENCE NO.: 60:5516e-h,5517a-b
TITLE: Antimicrobial imides
PATENT ASSIGNEE(S): Smith Kline & French Laboratories.
SOURCE: 11 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 932644		19630731	GB	
FR 1344172			FR	

PRIORITY APPLN. INFO.: US 19600815
GI For diagram(s), see printed CA Issue.
AB A number of imido derivs. of 6-aminopenicillanic acid and 7-aminocephalosporanic acid (Ia) are described. The Na salt (I) of cephalosporin C (4 g.) is dissolved in 60 ml. H2O and the pH adjusted to 2.5 by addn. of the acid form of Dowex 50 (x8). The resin is filtered off, washed with 20 ml. H2O, and the combined filtrate and washings are added to 20.5 ml. 0.1N HCl. After 72 hrs. at 20.degree., the mixt. is fractionated over Dowex-1 (acetate form) to yield 7-aminocephalosporanic acid and 3-hydroxymethyl-7-aminodecephalosporanic acid lactone (II). I (1 g.) in 50 ml. H2O adjusted with Dowex 50 (x8) to pH 2.6. the resin filtered off, the filtrate added to 3.8 ml. C5H6N, the soln. kept 48 hrs. at 37.degree., freeze-dried, the residue rubbed with Me2CO, redried, and the residue dissolved in 10 ml. H2O and fractionated as above gave the pyridinium inner salt of deacetylcephalosporin C (III). III subjected to the usual acid hydrolysis yielded 3-pyridiniummethyl-7-aminocephalosporanic acid inner salt. Ac2O (204 g.) and 200 g. 4-chlorophthalic acid heated until the solid dissolved and then for an addnl. 15 min. gave 4-chlorophthalic anhydride (IV). A mixt. of 130 ml. 28% NH3 and 182 g. IV refluxed 1.5-2 hrs. at 300.degree. gave 4-chlorophthalimide (V). To a stirred soln. of 90 g. V, 69 ml. Et3N, and 1 ml. Me2NCHO is slowly added 47.6 ml. ClCO2Et at -5.degree., and the mixt. stirred 30 min. at 0.degree. to yield N-carbethoxy-4-chlorophthal imide (VI). To 30 ml. H2O at room temp. are added 4.32 g. 6-aminopenicillanic acid, 5.75 g. Na2CO3, and 5.06 g. VI, and the mixture is stirred 20 min. to yield 6-(4-chlorophthalimido)penicillanic acid. Similarly were prepd. other 6-imidopenicillanic acids and 7-imidocephalosporanic acids (no phys. data given). Starting with II there was similarly obtained 3-hydroxymethyl-7-succinimidodecephalosporanic acid lactone. Other examples of 7-imido-3-hydroxymethyldecephalosporanic acid lactones were given.

09/ 076,574

Acetylesterase obtained from orange peels is added to 1 g. 7-phthalimidocephalosporanic acid in 15 ml. H2O, and the pH adjusted to 6 and kept at this level for 15 hrs. The soln. is then passed through an IR 4B column (acetate form), eluted with aq. 0.1M AcOH adjusted to pH 5.5 with pyridine, the eluant adjusted to pH 8 with dil. NaOH, and evapd. to yield the Na salt of 3-hydroxymethyl-7-phthalimidodecephalosporanic acid (VII). VII (1 g.) in 10 ml. collidine and 5 ml. EtCOCl is kept 10 hrs. to yield 3-propionyloxymethyl-7-phthalimidodecephalosporanic acid. Other esters were similarly obtained. These compds. have a high resistance to penicillinase and maintain their anti-microbial activity for a prolonged period of time.

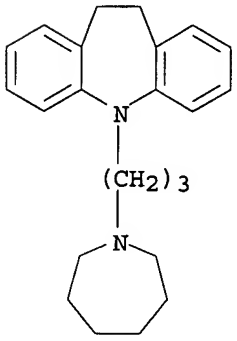
IT **2056-38-4**, Ethanesulfonic acid, compd. with 5-[3-(hexahydro-1H-azepin-1-yl)propyl]-10,11-dihydro-5H-dibenz[b,f]azepine
(prepn. of)

RN 2056-38-4 CAPLUS

CN Ethanesulfonic acid, compd. with 5-[3-(hexahydro-1H-azepin-1-yl)propyl]-10,11-dihydro-5H-dibenz[b,f]azepine (9CI) (CA INDEX NAME)

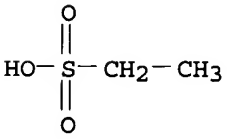
CM 1

CRN 2056-37-3
CMF C23 H30 N2



CM 2

CRN 594-45-6
CMF C2 H6 O3 S



L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1963:448385 CAPLUS
DOCUMENT NUMBER: 59:48385
ORIGINAL REFERENCE NO.: 59:8750a-h,8751a-f
TITLE: The development of psychotropic agents. IV. Diphenylamine derivatives with piperidyl-substituted side chains
AUTHOR(S): Stach, K.; Thiel, M.; Bickelhaupt, F.
CORPORATE SOURCE: Firma C. F. Boehringer Soehne G.m.b.H., Mannheim-Waldhof, Germany

09/ 076,574

SOURCE: Monatshefte fuer Chemie (1962), 93(5), 1090-1106
CODEN: MOCMB7; ISSN: 0026-9247
DOCUMENT TYPE: Journal
LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB cf. CA 59, 6389e. A 4-piperidone HCl (1 mole) in 2 l. C6H6, 2 moles secondary alc., and 2 g. p-Me-C6H4SO3H was refluxed until no more H2O distd., the C6H6 soln. decanted, the residue treated with 1 l. CHCl3 and then with 120 g. K2CO3 and 120 ml. H2O with stirring, the CHCl3 layer sepd., the aq. soln. extd. several times with CHCl3, and the combined CHCl8 exts. evapd. to give I (R, R1, X, % yield, and b.p. given); H, H, CH2CH2, 80, b26 108-10.degree.; H, H, (CH2)3, 72, b20 118-20.degree.; H, H, CH2CHCH2OH, 58, b13 175-7.degree.; Me, H, CH2CH2, 28, b0.2 60-2.degree.; Me, Me, CH2CH2, 67, b0.2 50-2.degree.. A soln. of 0.1 mole substituted alkyl chloride and 0.12 mole I in 200 ml. butanone or Et2CO was treated with 0.15 mole alkali carbonate and 0.5 g. NaI, the mixt. refluxed 8-10 hrs., filtered, the filtrate evapd. to dryness, the residue dissolved in Et2O, extd. at 0-10.degree. with 5-10% AcOH, the acid ext. alkalized, and extd. with Et2O to give II (R, X, Y, % yield, m.p. or b.p., and m.p. HCl salt given): H, (CH2)2, -, 67, 100-1.degree., 229-31.degree.; H, (CH2)3, -, 65, 82-4.degree., 154-5.degree.; H, (CH2)2, S, 81, 116-18.degree., 195.degree.; H, (CH2)2, S, 74, 132-3.degree., 193-4.degree.; H, (CH2)2, CH2OH, S, 37, 117-18.degree., -; H, (CH2)2, S (the piperidine ring is 2,6-Me2 disubstituted), 27, b0.2 278-82.degree., 140-1.degree.; Cl, (CH2)2, S, 83, b0.2 280-90.degree., 151-2.degree.; OMe, (CH2)2, S, 73, 80-2.degree., -; H, (CH2)2, O, 81, 103-5.degree., 212-13.degree.; H, (CH2)2, CH2CH2, 70, -, 205-6.degree.; H, (CH2)2, CH:CH, 69, 102-3.degree., 206-8.degree.. III (R and Y as for II) (0.1 mole) and 0.1 mole NaNH2 or NaH in 200 ml. abs. PhMe refluxed 4 hrs., treated with 0.1 mole 1-(3-chloropropyl)-4-piperidone ethylene ketal, refluxed 6-8 hrs., decompd. with H2O, extd. with dil. AcOH, and worked up as usual also gave II. 1-(2-Ethoxycarbonylethyl)-4-piperidone-HCl (26 g.), 9 g. glycol, 300 ml. abs. C6H6, and 0.5 ml. concd. H2SO4 refluxed until no more H2O was collected, the mixt. cooled to 0.degree., poured into concd. Na2CO8 soln., the C6H6 sepd., washed with H2O, dried, and distd. gave 82% the ethylene ketal (IV), b0.2 113-16.degree.; HCl salt m. 159-60.degree.. IV in Et2O reduced with LiAlH4 gave 85% 1-(3-hydroxypropyl)-4-piperidone ethylene ketal (V), m. 86-7.degree., also prepd. in 72% yield by refluxing 42.5 g. 4-piperidone ethylene ketal, 26.3 g. trimethylene chlorohydrin, 50 g. K2CO3, 1 g. NaI, and 250 cc. Et2CO 10 hrs. V with SOCl2 in refluxing C6H6 gave 97% 1-(3-chloropropyl)-4-piperidone ethylene ketal, b0.6 121-5.degree.; HCl salt m. 191-2.degree.. II.HCl dissolved in 10-15 parts H2O, treated with 2N HCl to Congo red, refluxed 8-12 hrs., alkalized, and extd. with Et2O or CH2Cl2 gave the free ketone (R, Y, % yield, m.p. or b.p., and m.p. HCl salt given): H, -, 78, -, 169-70.degree. (monohydrate); H, S (Va), 81, 78-80.degree., 88-90.degree. (monohydrate); H, S (the piperidine ring is 2,6-Me2 disubstituted), 92, -, 152-3.degree., Cl, S, 85, -, 102-4.degree. (monohydrate); OMe, S, 67, 93-5.degree., 80-90.degree. (monohydrate); H, O, 58, 86.degree., 190-2.degree.; H, CH2CH2, 75, b0.4 243-8.degree., 91-199.degree. (sic) (monohydrate); H, CH:CH, 60, 87-8.degree., 94-6.degree. (monohydrate). The free ketone was reduced with Raney Ni in MeOH, with LiAlH4 in Et2O, or with NaBH4 in MeOH to the 4-piperidinol analog (R, Y, % yield, m.p., and m.p. HCl salt given): H, -, 70, 92-3.degree., 233-4.degree.; Ac, -, 55, -, 192-3.degree. H, S, 82, -, 191-2.degree.; Cl, S, 70, 92-3.degree., -; OMe, S, 66, 93-4.degree., -; Ac, S, 82, -, 167-8.degree.; MeCHOH, S, 72, 155-6.degree., -; H, O, 79, -, 256-8.degree.; acetyl ethylene ketal, O, 65, 107-8.degree. -; Ac, O, 75, -, 240-2.degree.; H, CH2CH2, 73, -, 197-8.degree.; H, CH:CH, 60, -, 208-10.degree.. To a soln. of 3.5 g. Na in 350 cc. liquid NH8 in the presence of 0.5 g. FeCl3.6H2O was added 28.5 g. 2-acetylphenothiazine ethylene ketal, the mixt. stirred 1 hr., treated with 1-chloro-3-bromopropane, stirred 5 hrs., treated with 300 cc. Et2O, and allowed to evap. overnight gave 44-50% 2-acetyl-10-(3-

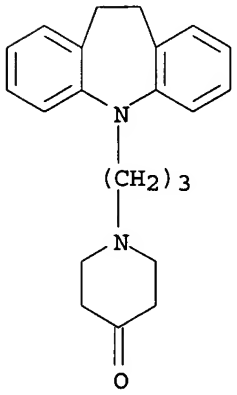
chloropropyl)phenothiazine ethylene ketal (VI), m. 87-9.degree.. VI (22 g.), 7.3 g. 4-piperidinol, 17 g. K2CO3, 1.1 g. 82% NaI, and 280 cc. Et2CO refluxed 8 hrs. under N gave 82% 2-acetyl-10-[3-(4-hydroxypiperidino)propyl]phenothiazine (VII) as HCl salt, m. 159-60.degree.. reduced with NaBH4 in alk. MeOH to the 2-(1-hydroxyethyl) analog of VII. m. 155-6.degree., in 72% yield. Treating 2-acetylphenoxazine ethylene ketal with NaNH2 in liquid NH3 and then with 1-chloro-3-bromopropane as above gave 54% 2-acetyl-10-(3-chloropropyl)phenoxazine (VIII) ethylene ketal, m. 82-4.degree. (Et2O-ligroine), hydrolyzed with alc. aq. HCl to 13-20% VIII, m. 90-3.degree.. VIII ethylene ketal, 4-piperidinol, K2CO8, and NaI in butanone as above gave 65% 3-(4-hydroxypiperidyl)propyl analog, m. 107-8.degree., hydrolyzed with 2N HCl to 75% 2-acetyl-10[3-(4-hydroxypiperidyl)propyl]phenoxazine, m. 164-5.degree.; HCl salt m. 239-41.degree. (alc.). 4-Methoxypyridine (140 g.), 10 cc. MeOH, and 10 cc. H2O with 0.5 g. Ru2O4 under an initial pressure of 150 atm. H was slowly heated to 140.degree., at which temp. redn. began. The temp. was kept below 150.degree. by cooling, redn. continued for 4 hrs., and the mixt. worked up to give 70-75% 4-methoxypiperidine, b. 163-6.degree.. Similarly were prepd. 4-ethoxy-(b. 174-6.degree.), 4-propoxy-(b. 196-8.degree.), and 4-isopropoxypiperidine, b. 184-6.degree.. By methods used for the prepn. of II were prepd. the following IX (R, R1, Y, % yield, m.p. or b.p., and m.p. HCl salt given): H, OMe, -, 70, 94-6.degree., -; H, OEt, -, 62, 66-7.degree., 180-1.degree.; Ac, OMe, 75, -, 100-5.degree. Ac, OEt, -, 72, -, 195-6.degree.; H, OMe, S (X), 75, -, 156-8.degree. H, OEt, S, 68,-, 156 7.degree.;-H, iso-PrO, S, 74, 155-7.degree.; H, PrO, S, 50, -, 156-8.degree.; Cl, OMe, S, b0.05 230-5.degree., -; OMe, OMe, S, 64, b0.1 235-40.degree., -; Ac, OMe, S, 83, -, 130-1.degree.; MeCHOH, OMe, S, 89, -; 124-6.degree.; Ac, OEt, S, 54, 233-40.degree./10-3 mm., -; H, OMe, O, 61, 45-7.degree., 192-3.degree.; H, OEt, O, 55, 58-60.degree., 198-200.degree.; Ac, OMe, O; 70, -, 177-9.degree.; Ac, OEt, O, 70, -, 198 200.degree.; H, OMe, CH2CH2, 60, -, 172-4.degree.; H, OMe, CH:CH, 63, -, 181-2.degree.. To a soln. of 13 g. IX (R = H, R1 = OH, Y = S) and 10 g. (iso-PrO)3Al in 100 cc. abs. dioxane was added over 8 hrs. CH2N2-Et2O (from 36 g. nitrosomethylurea). After several hrs. stirring, the soln. was poured into 2N HCl, the aq. layer alkalized, extd. with Et2O, Et2O distd., the residue dissolved in alc., and treated with (CO2H)2 to give 70% X oxalate, m. 185-6.degree.. To 200 cc. liquid NH3, 5.8 g. NaNH2, and 20 g. 2-acetylcarbazole in 100 cc. tetrahydrofuran (THF) stirred 1 hr. was added 22 g. 1-chloro-3-bromopropane and the mixt. stirred 6 hrs. with dry ice-cooling to give 57% 2-acetyl-9-(3-chloropropyl)carbazole, m. 99-101.degree.. To a hot soln. of 2.6 g. NH2OH.HCl in 50 cc. EtOH was added 10 g. Va to give 96% the oxime-HCl, m. 228-30.degree.; free base m. 112-14.degree.. Redn. of the oxime in THF with LiAlH4 gave 70% 1-[3-(10-phenothiazinyl) propyl]-4-aminopiperidine-2HCl (XI), m. 266-8.degree.. Va (10 g.) in 100 cc. MeOH was satd. with MeNH2 and then reduced with Raney Ni to give 76% the 4-methylamino analog of XI, m. 263-4.degree.. Similarly, with NH3, was prepd. XI. Redn. of 9.7 g. 1-[3(10-phenothiazinyl)propyl]-4-dimethylaminopyridinium chloride and 1 g. NaOH in 10 cc. MeOH with 8 g. NaBH4 in MeOH gave 82% 4-dimethylamino analog of XI, m. 284-6.degree.. 4-(2-Hydroxyethyl)piperidine (150 g.) and 500 cc. EtOH in the presence of 3 g. RuO2 was reduced in an autoclave at 90.degree. and 160-90 atm. H for 80 hrs. to give 94% crude 4-(2-hydroxyethyl)piperidine (XII), b0.2 101-11.degree.. By methods used for the prepn. of II, an alkyl chloride and XII gave the following IX (R1 = CH2CH2OH) (Y, R, % yield, m.p., and m.p. HCl salt given): -, H, 50, -, 188-9.degree.; -, Ac, 63, -, 100-3.degree.; S, H, 68, -, 182-3.degree.; S, Ac, 80, 98-100.degree., 100-10.degree.; O, H, 54, 109-10.degree., 150-2.degree.; O, Ac, 90, 114-15.degree., 215.degree.; O, acetyl ethylene ketal, 77, 106-7.degree. -. Similarly were prepd. the following IX (R1 = H) (Y, R, m.p. HCl salt, and % yield given): -, H, 221-3.degree., 74; -, Ac, 188-9.degree., 78; S, H, 176-7.degree., 40; S, Ac, 175-6.degree., 60; O, H, 199-200,% 70; O, Ac, 230-2.degree., 85 (prepd. via the ethylene

ketal, m. 80-1.degree.).

IT **51551-35-0**, 4-Piperidone, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]- **95434-01-8**, 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[3-(4-methoxypiperidino)propyl]- **100030-28-2**, 4-Piperidinol, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, hydrochloride **104811-00-9**, 5H-Dibenz[b,f]azepine, 5-[3-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-propyl]-10,11-dihydro-, hydrochloride **106784-65-0**, 4-Piperidone, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, hydrochloride
(prepn. of)

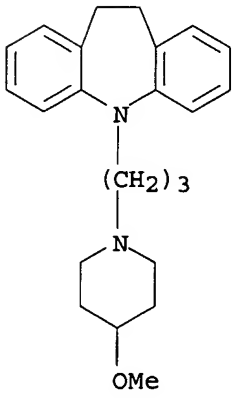
RN 51551-35-0 CAPLUS

CN 4-Piperidinone, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]- (9CI) (CA INDEX NAME)



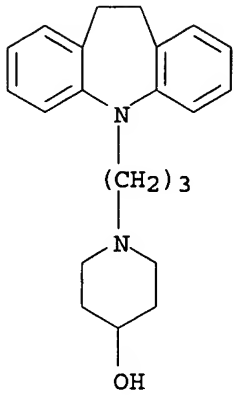
RN 95434-01-8 CAPLUS

CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[3-(4-methoxypiperidino)propyl]- (7CI) (CA INDEX NAME)



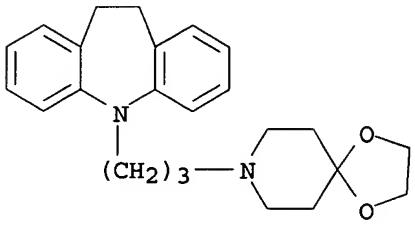
RN 100030-28-2 CAPLUS

CN 4-Piperidinol, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, hydrochloride (7CI) (CA INDEX NAME)



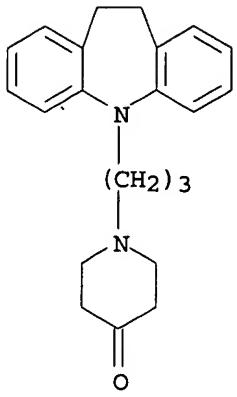
x HCl

RN 104811-00-9 CAPLUS
CN 5H-Dibenz[b,f]azepine, 5-[3-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)propyl]-10,11-dihydro-, hydrochloride (7CI) (CA INDEX NAME)



● HCl

RN 106784-65-0 CAPLUS
CN 4-Piperidone, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, hydrochloride (7CI) (CA INDEX NAME)



HCl

L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1963:8792 CAPLUS
DOCUMENT NUMBER: 58:8792
ORIGINAL REFERENCE NO.: 58:1439c-h,1440a-b
TITLE: Piperidine derivatives and their salts
PATENT ASSIGNEE(S): C. F. Boehringer & Soehne G.m.b.H.
SOURCE: 15 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 611302		19620608	BE	
FR 1332535			FR	
GB 923910			GB	

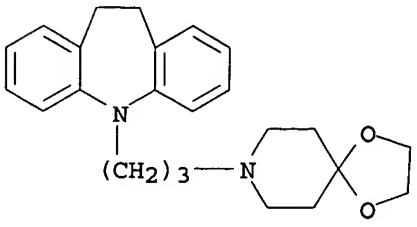
PRIORITY APPLN. INFO.: DE 19601209
GI For diagram(s), see printed CA Issue.
AB Compounds of formula I, where Q is phenoxazinyl, carbazolyl, acridanyl, iminodibenzylyl, or imino-stilbenyl attached to A by the N atom, A is a straight-or branched-chain C2-4 alkylene radical, and Y is O, (OH)H, or (OR)2 where R is lower alkyl or the two R groups may be joined as an alkylene chain, are prepd: by treating RAZ with the Y-substituted piperidine or RH with the Y-substituted N-(ZA)-substituted piperidine; ketals so obtained may be hydrolyzed to piperidones, which may be reduced to piperidinols. 4 - Piperidone 1,3-propylene ketal (36.5 g.), 7 g. NaI, 60 g. K2CO3, 48 g. 9-(.gamma.-chloropropyl)carbazole, and 700 ml. butanone was refluxed 8 hrs., the mixt. was filtered, the filtrate concd., and the residue recrystd. from MeOH to yield 47 g. 1-[.gamma.-(carbazol-9-yl)propyl]-4-piperidone 1,3-trimethylene ketal, m. 82-4.degree.; hydrochloride m. 154-5.degree.. The hydrochloride (10 g.) was refluxed 3 hrs. with 50 ml. 0.5N HCl, the cooled soln. made alk. with soda and extd. with Et2O, the solvent removed from the ext., and the residue dried in vacuo at 50-60.degree., taken up in abs. Et2O, and treated with HCl in Et2O to ppt. 6.85 g. 1-[.gamma.-(carbazol-9-yl)propyl]-4-piperidone hydrochloride monohydrate, m. 169-70.degree.. This (7 g.) in 100 ml. MeOH was hydrogenated with Raney Ni under pressure, the catalyst filtered off, the solvent removed, the residue dissolved in Et2O, pptd. with Et2O-HCl, and recrystd. from 2-propanol to give 7.3 g. 1-[.gamma.-(carbazol-9-yl)propyl]-4-piperidinol hydrochloride, m. 233-4.degree.. Similarly prepd. are 1-[.gamma.-(iminodibenzyl-5-yl)propyl]4-piperidone ethylene

ketal hydrochloride, m. 205-6.degree., and the corresponding piperidone hydrochloride hydrate (I), m. 77-85.degree.; 1 - [.gamma. -(phenoxazin-10-yl)propyl]-4-piperidone ethylene ketal, m. 104-5.degree. (hydrochloride m. 210-12.degree.), the corresponding piperidone, m. 86.degree. (hydrochloride m. 190-2.degree.), and the corresponding piperidinol hydrochloride, m. 255-8.degree.; and 1-[.gamma.-(carbazol-9-yl)propyl]-4-piperidone ethylene ketal, m. 100-1.degree.; hydrochloride m. 229-31.degree.. A soln. of 7 g. I in 20 ml. Et2O was added dropwise to a suspension of 1 g. Li alanate in 50 ml. Et2O, the mixt. refluxed 6 hrs., 4 ml. H2O added, the soln. filtered, dried over K2CO3, and neutralized with Et2O-HCl. The ppt. was filtered off, washed with Et2O, and dried to yield 6.6 g. 1-[.gamma.-(iminodibenzyl-5-yl)propyl]-4-piperidinol hydrochloride hydrate, m. 100-3.degree.. PhBr (12 g.) was added to a suspension of 0.55 g. Li in 50 ml. Et2O, the soln. refluxed, 14 g. acridan added, and the soln. stirred 2 hrs. 1-(.gamma.-Chloropropyl)-4-piperidone ethylene ketal (17 g.) was added dropwise, the soln. stirred 2 hrs., H2O added, the ether layer sepd., the aq. layer extd. with Et2O, the Et2O removed from the soln. and exts., and the residue recrystd. from MeOH to yield 19 g. 1-[.gamma.-(acridan-10-yl)propyl]-4-piperidone ethylene ketal, m. 137-8.degree.; hydrochloride m. 200.degree.. 1-[.gamma.-(Imino-stilben-5-yl)propyl]-4-piperidone ethylene ketal, m. 102-3.degree. (hydrochtoride m. 205-8.degree.), was prepd. similarly, and is hydrolyzed to the corresponding piperidone (II), m. 87-8.degree.; hydrochloride hydrate m. 94-6.degree.. II (10 g.) in 300 ml. Et2O was reduced with LiAlH4 to the corresponding piperidinol, m. 63-5.degree. (2-propanol-Et2O); hydrochloride (8.5 g.) m. 208-10.degree.. The above compds. had neuroleptic, thymoleptic, or thymeretic effects. N-(.gamma.-Chloropropyl)carbazole, -imidodibenzyl, and -phenoxazine were prepd. from the corresponding Li compds. and p-MeC6H4SO3CH2CH2CH2Cl. 4-Piperidone ethylene ketal (III), b26 108-10.degree., were prepd. from 4-piperidone and ethylene glycol; 4-piperidone 1,3-propylene ketal, b20 118-20.degree., and 1-(.beta.-carbethoxyethyl)-4- piperidone ethylene ketal (IV), b0.5 152-5.degree. were prepd. similary. III was treated with ClCH2CH2CH2OH and IV is reduced with LiAlH4, to yield 1-(.gamma.-hydroxypropyl)-4-piperidone ethylene ketal, b0.3 120-5.degree., m. 87-8.degree., which with SOCl2 gave 1-(.gamma.-chloropropyl)-4-piperidone ethylene ketal hydrochloride, m. 190-2.degree.;the free base b0.6 120-5.degree.. This was also obtained from III and BrCH2CH2CH2Cl.

IT **104811-00-9**, 5H-Dibenz[b,f]azepine, 5-[3-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-propyl]-10,11-dihydro-, hydrochloride
106066-71-1, 4-Piperidinol, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, hydrochloride, hydrate
106784-62-7, 4-Piperidone, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, hydrochloride, hydrate
(prepn. of)

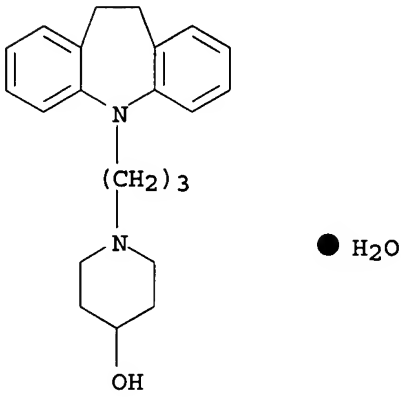
RN 104811-00-9 CAPLUS

CN 5H-Dibenz[b,f]azepine, 5-[3-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)propyl]-10,11-dihydro-, hydrochloride (7CI) (CA INDEX NAME)



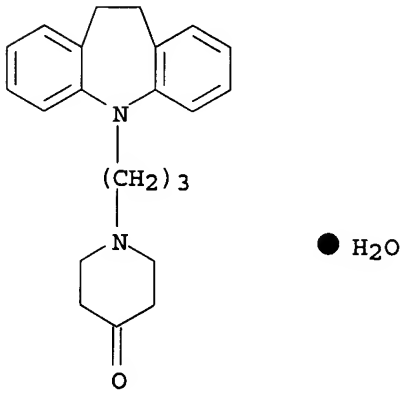
HCl

RN 106066-71-1 CAPLUS
CN 4-Piperidinol, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, hydrochloride, hydrate (7CI) (CA INDEX NAME)



HCl

RN 106784-62-7 CAPLUS
CN 4-Piperidone, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, hydrochloride, hydrate (7CI) (CA INDEX NAME)



HCl

L4 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1962:469319 CAPLUS
DOCUMENT NUMBER: 57:69319
ORIGINAL REFERENCE NO.: 57:13785e,13786a-e
TITLE: N-Heterocyclic compounds
INVENTOR(S): Dietrich, Henri
PATENT ASSIGNEE(S): Geigy Chemical Corp.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3040031		19620619	US	
CH 374074			CH	
DE 1186864			DE	

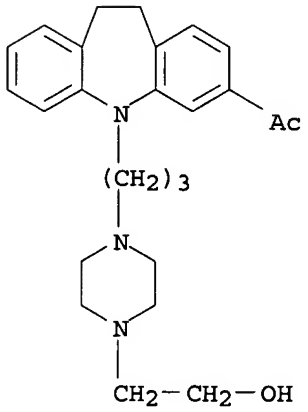
PRIORITY APPLN. INFO.: CH 19590723

AB The title compds. are 3-acyl10,11-dihydro-5H-dibenz[b,f]azepines substituted in the 5-position by a basic radical. 5-Acetyliminobibenzyl (I) 119 and AcCl 150 in CS2 300 were added dropwise to AlCl3 300 in CS2 600 parts by vol. The mixt. was kept 1 hr., refluxed 16 hrs., cooled, CS2 decanted, and the residue poured onto ice 600 and concd. HCl 12 parts to give 3,5-diacetyliminobibenzyl (II), m. 143-4.degree.. II was refluxed 6 hrs. in alc. KOH (28 g. KOH in 300 cc. alc.) to give 3-acetyliminobibenzyl (III), m. 157.degree.; dinitrophenylhydrazone m. 240.degree.. III 23.7 in anhyd. xylene 250 was refluxed 70 hrs. with ethylene glycol 20 and p-MeC6H4SO3H 0.05 part, with water used as a separator, to give 3-(.alpha.,.alpha.-ethylenedioxyethyl)- iminobibenzyl (IV), m. 134-6.degree.. IV 28.1 with NaNH2 4.3 in xylene at 90-100.degree. gave the Na salt which was treated with .gamma.-dimethylaminopropyl chloride (prepd. from the HCl salt 16 parts) and the mixt. refluxed 20 hrs. to give after decompn. of the ketal 3-acetyl-5-(.gamma.-dimethylaminopropyl)iminobibenzyl, b0.01 175-6.degree.; HCl salt m. 191.degree.. Similarly, from IV were prepd. the following iminobibenzyls: 5-(.gamma.-dimethylaminopropyl)-3-propionyl-, b0.05 180-4.degree. 3-acetyl-5(.gamma.-hexamethylenimino-.beta.-methylpropyl)-, b0.003 211.degree. HCl salt m. 191-3.degree.; 3-acetyl-5-[.gamma.-(4-formylpiperazin-1-yl)- propyl]-, which with .gamma.NaOH-MeOH-H2O gave 3-acetyl-5[.gamma.-piperazin-1-ylpropyl]-; 3-acetyl-5-(.beta.-piperidinoethyl)-, HCl salt m. 206.degree.; and 3-acetyl-5-(1-methylpiperid-2-ylethyl)-, b0.06 195.degree.. The Na salt of IV with dimethylaminoisopropyl chloride gave a mixt. of 3-acetyl-5-(.beta.-dimethylamino-.beta.-methyl)ethyl- and 3-acetyl-5-(.beta.-dimethylamino.alpha.-methyl)ethyliminobibenzyl, HCl salt m. 207-8.degree.. Similarly prepd. from IV was 5-(.gamma.-chloropropyl)-3-(.alpha.,.alpha.-ethyl- enedioxyethyl)iminobibenzyl (V). V 12.8 with 1-(.beta.-hydroxyethyl)piperazine 6.5 and 2-butanone 65 parts by vol. were refluxed 16 hrs. to give 3-acetyl-5-[.gamma.-[4-(.beta.-hydroxyethyl)piperazin-1-yl]propyl]iminobibenzyl (VI), bishemioxalate salt m. 209-10o (decompn.). VI bishemioxalate salt m. 209-10.degree. (decompn.). VI was acetylated to give 3- acetyl-5-[.gamma.-[4-(.beta.-acetoxyethyl)piperazin-1-yl]propyl]iminobibenzyl (VII), bishemioxalate salt m. 207-9.degree. (decompn.). VIIw as also prepd. from V and 1-(.beta.-acetoxyethyl)piperazine. VI was treated with **propionic** anhydride in C5H5N to give 3-acetyl-5-[.gamma.-(4-(.beta.-propionyloxyethyl)piperazin-1-yl]propyl]iminobibenzyl. V with alc. MeNH2 at 80.degree. 16 hrs. in a closed system gave 3-acetyl-5-(.gamma.-methylaminopropyl)iminobibenzyl, b0.04 179-83.degree., also prepd. from IV and .gamma.-(Nformylmethylamino)propyl chloride. The title compds. have varied pharmacological properties, including sedative action, and can be used as potentiators of anesthetics.

IT **1838-01-3**, Ketone, 10,11-dihydro-5-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-5H-dibenz[b,f]azepin-3-yl methyl **1838-25-1**, Ketone, 10,11-dihydro-5-[2-(1-methyl-2-piperidyl)ethyl]-5H-dibenz[b,f]azepin-3-yl methyl **101058-63-3**, Ketone, 10,11-dihydro-5-[3-(1-piperazinyl)propyl]-5H-dibenz[b,f]azepin-3-yl methyl **101520-44-9**, Ketone, 10,11-dihydro-5-[3-(4-methyl-1-piperazinyl)propyl]-5H-dibenz[b,f]azepin-3-yl methyl **101547-02-8**, Ketone, 10,11-dihydro-5-[3-(4-methyl-1-piperazinyl)propyl]-5H-dibenz[b,f]azepin-3-yl methyl, dihydrochloride **102324-36-7**, Ketone, 10,11-dihydro-5-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-5H-dibenz[b,f]azepin-3-yl methyl, acetate **104298-64-8**, Ketone, 10,11-dihydro-5-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-5H-

dibenz[b,f]azepin-3-yl methyl, dioxalate **104442-94-6**, Ketone, 10,11-dihydro-5-(2-methyl-3-piperidinopropyl)-5H-dibenz[b,f]azepin-3-yl methyl, hydrochloride **104551-27-1**, Ketone, 10,11-dihydro-5-(2-methyl-3-piperidinopropyl)-5H-dibenz[b,f]azepin-3-yl methyl **105044-46-0**, Ketone, 10,11-dihydro-5-(2-piperidinoethyl)-5H-dibenz[b,f]azepin-3-yl methyl, hydrochloride **106764-49-2**, 1-Piperazinecarboxaldehyde, 4-[3-(3-acetyl-10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-
(prepn. of)

RN 1838-01-3 CAPLUS
CN Ketone, 10,11-dihydro-5-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-5H-dibenz[b,f]azepin-3-yl methyl (7CI, 8CI) (CA INDEX NAME)



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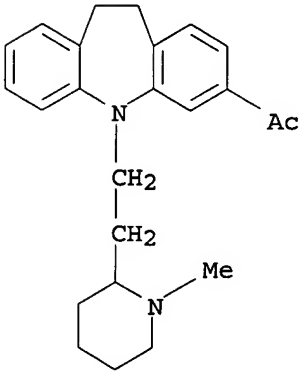
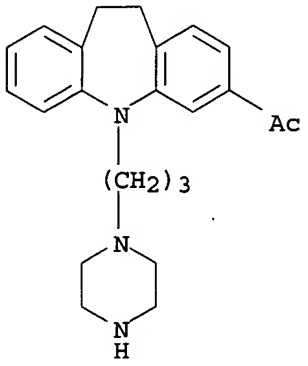
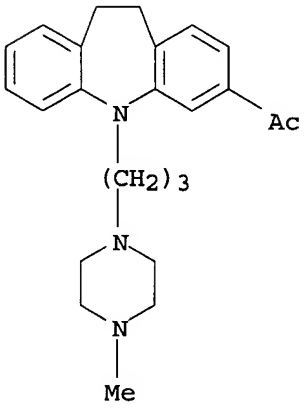


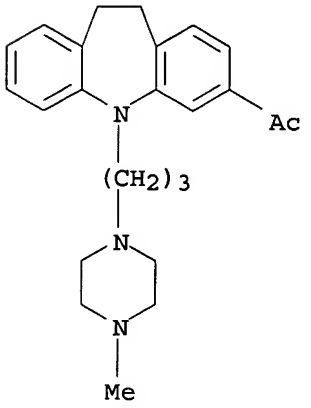
RN 101058-63-3 CAPLUS
CN Ketone, 10,11-dihydro-5-[3-(1-piperazinyl)propyl]-5H-dibenz[b,f]azepin-3-yl methyl (7CI) (CA INDEX NAME)



RN 101520-44-9 CAPLUS
CN Ketone, 10,11-dihydro-5-[3-(4-methyl-1-piperazinyl)propyl]-5H-dibenz-[b,f]azepin-3-yl methyl (7CI) (CA INDEX NAME)

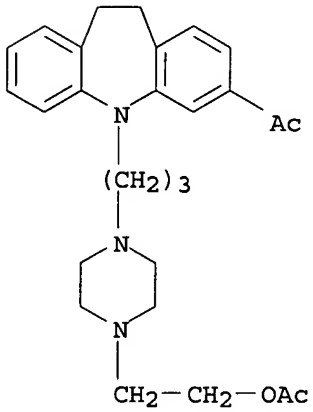


RN 101547-02-8 CAPLUS
CN Ketone, 10,11-dihydro-5-[3-(4-methyl-1-piperazinyl)propyl]-5H-dibenz-[b,f]azepin-3-yl methyl, dihydrochloride (7CI) (CA INDEX NAME)



●2 HCl

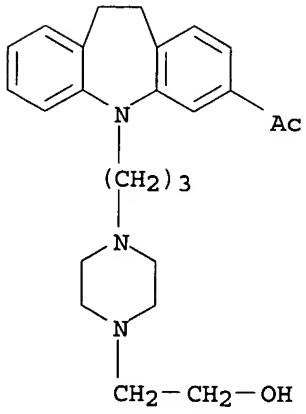
RN 102324-36-7 CAPLUS
CN Ketone, 10,11-dihydro-5-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-5H-dibenz[b,f]azepin-3-yl methyl, acetate (7CI) (CA INDEX NAME)



RN 104298-64-8 CAPLUS
CN Ketone, 10,11-dihydro-5-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-5H-dibenz[b,f]azepin-3-yl methyl, dioxalate (7CI) (CA INDEX NAME)

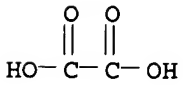
CM 1

CRN 1838-01-3
CMF C25 H33 N3 O2



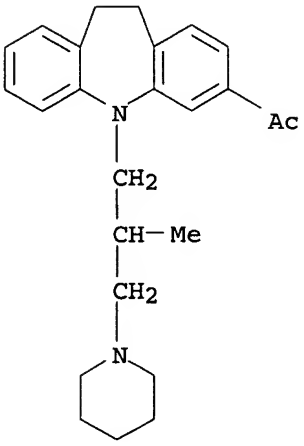
CM 2

CRN 144-62-7
CMF C2 H2 O4



RN 104442-94-6 CAPLUS
CN Ketone, 10,11-dihydro-5-(2-methyl-3-piperidinopropyl)-5H-dibenz[b,f]azepin-

3-yl methyl, hydrochloride (7CI) (CA INDEX NAME)



● HCl

RN 104551-27-1 CAPLUS
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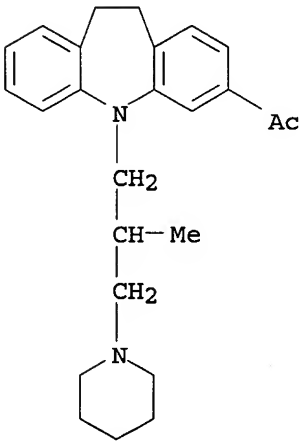
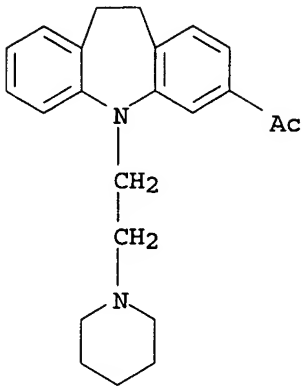
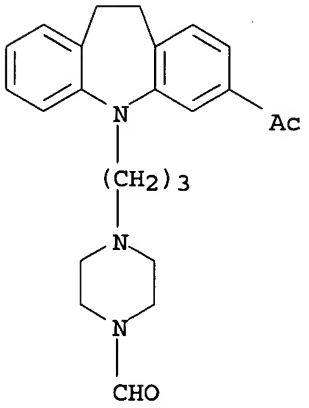


RN 105044-46-0 CAPLUS
CN Ketone, 10,11-dihydro-5-(2-piperidinoethyl)-5H-dibenz[b,f]azepin-3-yl methyl, hydrochloride (7CI) (CA INDEX NAME)



x HCl

RN 106764-49-2 CAPLUS
CN 1-Piperazinecarboxaldehyde, 4-[3-(3-acetyl-10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]- (7CI) (CA INDEX NAME)

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L2          1920 S L1 FUL

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L4            12 S L3 AND PROPIONIC

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       1376112 'B'
        540143 'F'
          4299 'AZEPIN'
             0 'BENZO[B,F]AZEPIN'
                 ('BENZO'(W)'B'(W)'F'(W)'AZEPIN')
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=> s l3 not 'dibenz[b,f]azepin'
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        540143 'F'
          4299 'AZEPIN'
           221 'DIBENZ[B,F]AZEPIN'
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=> s l6 and propionic
         49428 PROPIONIC
L7             6 L6 AND PROPIONIC

=> d l7 1- ibib abs fhitstr
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L7   ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2000:756706  CAPLUS
DOCUMENT NUMBER:          133:321882
TITLE:                    Preparation of substituted fused imidazoles for
                          treatment and/or prevention of diseases and disorders
                          related to the histamine H3 receptor
INVENTOR(S):              Dorwald, Florencio Zaragoza; Andersen, Knud Erik;
                          Jorgensen, Tine Krogh; Peschke, Bernd; Wulff, Birgitte
                          Schjellerup; Pettersson, Ingrid; Rudolf, Klaus;
                          Stenkamp, Dirk; Hurnaus, Rudolf; Muller, Stephan
                          Georg; Krist, Bernd
PATENT ASSIGNEE(S):       Novo Nordisk A/S, Den.; Boehringer Ingelheim
                          International, G.m.b.H.
SOURCE:                   PCT Int. Appl., 169 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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     WO 2000063208      A1   20001026       WO 2000-DK179    20000413
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
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             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1173438         A1   20020123       EP 2000-918714   20000413
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     JP 2002542245      T2   20021210       JP 2000-612298   20000413
PRIORITY APPLN. INFO.:                   DK 1999-508      A  19990416
                                         DK 1999-1345     A  19990922
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OTHER SOURCE(S):          MARPAT 133:321882
GI
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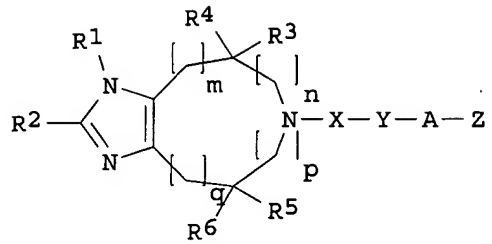

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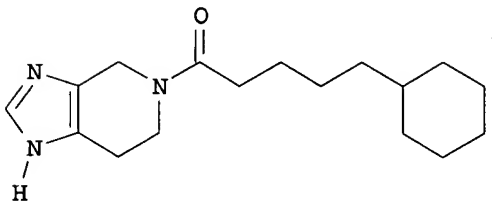


II

AB The title compds. [I; R1 = H, a functional group which can be converted to H in vivo; R2 = H, alkyl, halo, etc.; R3-R6 = H, CO2H, alkoxycarbonyl, etc.; m, n, p, q = 0-2; X = a bond, CH2, CO, etc.; Y = a bond, O, NR12 (R12 = H, alkyl, aryl, etc.); A = a bond, alkylene, alkenylene, etc.; Z = R13, OR13, SR13, etc. (R13 = H, alkyl, aryl, etc.)], useful for the treatment and/or prevention of diseases and disorders related to the histamine H3 receptor (more particularly, useful for the treatment and/or prevention of diseases and disorders, in which an interaction with the histamine H3 receptor is beneficial), were prepd. and formulated. E.g., treatment of 5-cyclohexylpentanoic acid with carbonyldiimidazole in DCM followed by addn. of 4,5,6,7-tetrahydroimidazo[4,5-c]pyridine in DCM afforded 24% II. Compds. I are effective at 0.05-10 mg/kg/day.

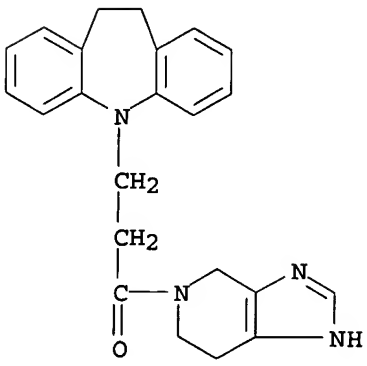
IT **303019-87-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of substituted fused imidazoles for treatment and/or prevention of diseases and disorders related to the histamine H3 receptor)

RN 303019-87-6 CAPLUS

CN 1H-Imidazo[4,5-c]pyridine, 5-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)-1-oxopropyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:34896 CAPLUS
DOCUMENT NUMBER: 130:110162
TITLE: Preparation of N-substituted azaheterocyclic compounds for the clinical treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiological role
INVENTOR(S): Andersen, Knud Erik; Jorgensen, Tine Krogh; Hohlweg, Rolf; Fischer, Erik; Olsen, Uffe Bang; Polivka, Zdenek; Sindelar, Karel; Valenta, Vladimir
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9900367	A1	19990107	WO 1998-DK273	19980622
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6040318	A	20000321	US 1998-98579	19980617
AU 9879074	A1	19990119	AU 1998-79074	19980622
EP 991621	A1	20000412	EP 1998-929235	19980622
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JP 2002515914	T2	20020528	JP 1999-505222	19980622
ZA 9805448	A	19990119	ZA 1998-5448	19980623
US 6066632	A	20000523	US 1999-376735	19990817
US 6100253	A	20000808	US 1999-376734	19990817
US 6114354	A	20000905	US 1999-375745	19990817

PRIORITY APPLN. INFO.:
DK 1997-751 A 19970625
US 1997-51833P P 19970707
US 1998-98579 A3 19980617
WO 1998-DK273 W 19980622

OTHER SOURCE(S): MARPAT 130:110162
GI

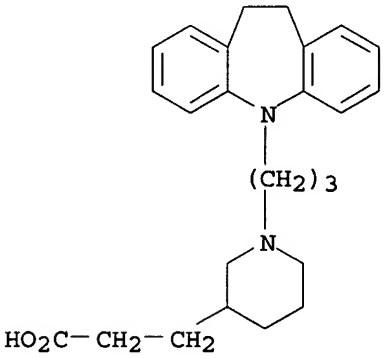
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1, R2 = H, halo, CF3, etc.; Y = >N-CH2-, >CH-CH2-, >C:CH- (only the first atom participates in the ring system); X = o-phenylene, O, S, etc.; r = 1-3; Z = II-V (wherein R3 = (CH2)pCO2H; p = 2-6)] and their salts, useful for the clin. treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role by eliciting neurogenic pain or inflammation as well as their use for treatment of indications caused by or related to the secretion and circulation of insulin antagonizing peptides, e.g. non-insulin-dependent diabetes mellitus (NIDDM) and ageing-assocd. obesity, were prepd. and formulated. Thus, reaction of 5-(3-bromo-1-propylidene)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene with

3-(piperidin-3-yl)**propionic** acid Et ester (prepn. given) in the presence of K2CO3 in DMF followed by hydrolysis of the resulting ester afforded VI.HCl which showed 42% inhibition of histamine induced hyperglycemia at 1.0 mg/kg.

IT **219608-69-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-substituted azaheterocyclic compds. for the clin. treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role)

RN 219608-69-2 CAPLUS
CN 3-Piperidinepropanoic acid, 1-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:28656 CAPLUS
DOCUMENT NUMBER: 128:102008
TITLE: Preparation and formulation of pyridine derivatives as antitumor agents and immunosuppressants
INVENTOR(S): Biedermann, Elfi; Hasmann, Max; Loser, Roland; Rattel, Benno; Reiter, Friedemann; Schein, Barbara; Seibel, Klaus; Vogt, Klaus
PATENT ASSIGNEE(S): Klinge Pharma G.m.b.H., Germany; Biedermann, Elfi; Hasmann, Max; Loser, Roland; Rattel, Benno; Reiter, Friedemann; Schein, Barbara; Seibel, Klaus; Vogt, Klaus
SOURCE: PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9748397	A1	19971224	WO 1997-EP3244	19970620

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,

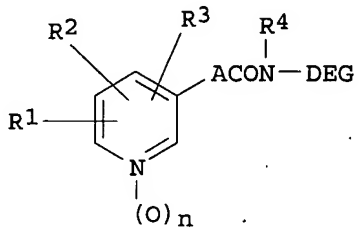
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

DE 19624668	A1	19980219	DE 1996-19624668	19960620
ZA 9705443	A	19980210	ZA 1997-5443	19970619
AU 9732624	A1	19980107	AU 1997-32624	19970620
EP 912176	A1	19990506	EP 1997-928260	19970620
EP 912176	B1	20020925		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000512652	T2	20000926	JP 1998-502317	19970620
AT 224713	E	20021015	AT 1997-928260	19970620
ES 2181006	T3	20030216	ES 1997-928260	19970620
US 6451816	B1	20020917	US 1998-216482	19981218

PRIORITY APPLN. INFO.: DE 1996-19624668 A 19960620
WO 1997-EP3244 W 19970620

OTHER SOURCE(S): MARPAT 128:102008

GI



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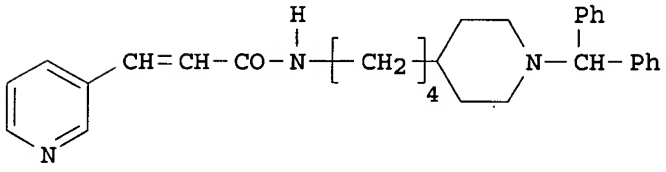


II

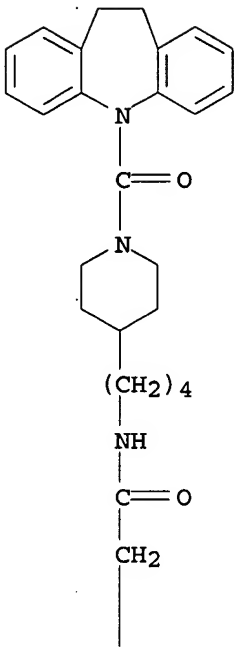
AB The title compd. I [R1 = H, halo, cyano, etc.; R2 = H, halo, hydroxy, alkyl, etc.; R3 = H, halo, alkyl, etc.; R4 = H, hydroxy, benzyloxy, etc.; n = 0 or 1; A = alkylene, etc.; D = alkylene, etc.; E = piperidine ring (generic structure given), etc.; G = H, etc.] are prepd. The title compd. II in vitro showed IC50 of 0.008 .mu.M against the WERI-Rb-1 retinoblastoma cells.

IT **200868-28-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyridine derivs. as antitumor agents and immunosuppressants)

RN 200868-28-6 CAPLUS

CN 3-Pyridinepropanamide, N-[4-[1-[(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)carbonyl]-4-piperidinyl]butyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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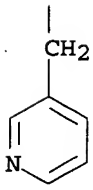
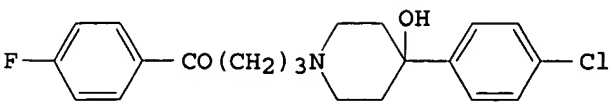


L7 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1988:1685 CAPLUS
DOCUMENT NUMBER: 108:1685
TITLE: A rapid and simplified extraction of haloperidol from plasma or serum with Bond Elut C18 cartridge for analysis by high performance liquid chromatography
AUTHOR(S): Hayakari, Makoto; Hashimoto, Yumiko; Kita, Takeshi; Murakami, Satoshi
CORPORATE SOURCE: Sch. Med., Hirosaki Univ., Hirosaki, 036, Japan
SOURCE: Forensic Science International (1987), 35(1), 73-81
CODEN: FSINDR; ISSN: 0379-0738
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



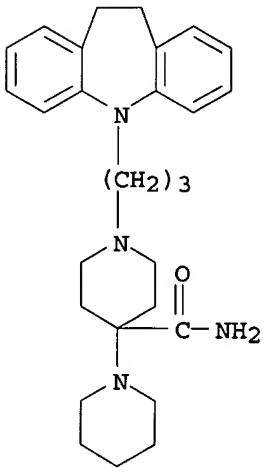
I

AB A method for the detn. of haloperiodol (HAL) (I) in plasma is based on HPLC with a reversed-phase column, ODS-C18. HAL is rapidly extd. from human plasma by using a Bond Elut C18 cartridge and its recovery is >90%. The mobile phase is a mixt. of 1% acetate/MeCN/tetrahydrofuran/triethylamine (69.5:28.2:1.9:0.4, by vol.). The method is rapid, simple, and free from interferences and gives good precision.

IT **5942-95-0**, Carpipramine
RL: ANT (Analyte); ANST (Analytical study)
(HPLC of)

RN 5942-95-0 CAPLUS

CN [1,4'-Bipiperidine]-4'-carboxamide, 1'-[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]- (7CI, 8CI, 9CI) (CA INDEX NAME)



L7 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1968:95776 CAPLUS
DOCUMENT NUMBER: 68:95776
TITLE: Phenothiazine derivatives. VII. Preparation of selectively acting phenothiazine derivatives
AUTHOR(S): Toldy, Lajos; Toth, Istvan; Borsy, Jozsef
CORPORATE SOURCE: Inst. Arzneimittelforsch., Budapest, Hung.
SOURCE: Acta Chimica Academiae Scientiarum Hungaricae (1967), 53(3), 279-94
CODEN: ACASA2; ISSN: 0001-5407
DOCUMENT TYPE: Journal
LANGUAGE: German

GI For diagram(s), see printed CA Issue.

AB A no. of phenothiazines were prepd. that showed significant antiulcerogenic and coronary-enlargening activity and in certain cases selectively. The compds. tested are those listed in the table (Ia) and in the following 3 series. Series A, 3-substituted (R)-10-substituted(R')phenothiazines [R, R', no., and m.p. (deriv.) given]: H, PhCH2CHMeNH(CH2)3, XVIII, 185.degree. (oxalate); Cl, PhCH2CHMeNH(CH2)3, XIX, 159-60.degree. (hydrochloride); Cl, PhCH2CHMeNMe(CH2)3, XX, 175.degree. (oxalate); H, PhCH2CHMeNHCOCH2CH2, XXI, 121-3.degree.; Cl, PhCH2CHMeNHCOCH2CH2, XXII, 111-13.degree.. Series B, 5-substituted (R)-iminodibenzyls [R, no., and m.p. (deriv.) given]: o-xylyl, XXIII, 197-200.degree. (difumarate); 3-[4-(2-phenylisopropyl)-1-piperazinyl] propionyl, XXIV, 208-10.degree. (difumarate); 3-[4-(2-phenylisopropyl)-1-piperazinyl]ethyl, XXV, 252-4.degree. (dihydrochloride); PhCH2CHMeNH(CH2)3, XXVI, 188-91.degree. (oxalate); PhCH2CHMeNMeCH2CH2,

XXVII, 173-5.degree. (oxalate). Series C, PhCH2CHMeR [R, no., and m.p. (deriv.) or b.p. given]: morpholino, XXVIII, b1 133.degree.; hexamethylenimino, XXIX, b0.5 120-30.degree.; heptamethylenimino, XXX, b0.8 165.degree.; 4-(benzyloxycarbonyl)-1-piperazinyl, XXXI, 153-5.degree. (fumarate); 4-(p-chlorobenzyloxycarbonyl)-1-piperazinyl, XXXII, 163-5.degree. (hydrochloride); 3,4,5-(MeO)3C6H2CONH, XXXIII, 164-6.degree.. Series C was pharmacol. uninteresting. III, VIII, and XX equaled and VI and XXVII exceeded the ulcer-arresting action of chloropromazine and chlorobenzoxamine, and the action of VI and XXVII was selective. Neither VI nor XXVII had anticholinergic activity. XIV showed strong, selective coronary-enlargening activity, while XV showed stronger tranquilizing action than methophenazine and at the same time an intense coronary-enlargening action. [TABLE OMITTED] 3-Trifluoromethylphenothiazine (34.5 g.) and 8.5 g. NaNH2 in PhMe was refluxed 2 hrs., treated at 60.degree. with 14 ml. propylene oxide in PhMe dropwise during 2 hrs., refluxed 2 hrs., and treated with MeOH and then H2O to give 16 g. 3-trifluoromethyl-10-.beta.-hydroxypropylphenothiazine (XXXIV), b0.2 168-72.degree.. XXXIV (20.5 g.) and 10.3 ml. mesyl chloride in pyridine yielded 23 g. (crude) 3-trifluoromethyl-10-.beta.-mesyloxypropylphenothiazine (XXXV), m. 108-10.degree. (1:1 C6H6-Me2CO). XXXV (20 g.) and 20 g. N-.beta.-hydroxyethylpiperazine in 200 ml. xylene was refluxed 8 hrs. and cooled, the soln. decanted from oil and washed with H2O, the xylene soln. extd. with 15% tartaric acid soln., the ext. basified, and the washed and dried syrup treated with fumaric acid in hot dry EtOH to give 10 g. XIII difumarate (EtOH). Similarly were prepd. II, III, IV, VI, IX, X, XVII, XXIII, XXIV, XXVIII, XXIX, and XXX (sometimes in C6H6, PhMe, or morpholine). Treatment of XIII in ClCH2CH2Cl with 3,4,5-(MeO)3C6H2COCl gave XIV. VII, XV, and .beta.-(3-chloro-10-phenothiazinyl)**propionic** acid [2-methoxy-4-(diethylcarbamoyl)]phenyl ester (m. 119-21.degree.) were prepd. similarly. XI and XII were prepd. by esterification in pyridine, Treatment of 5 g. PhCH2Ac and 8.7 g. 5-(.gamma.-aminopropyl)iminodibenzyl in EtOH with H and 6 g. Raney Ni at 60.degree. and 25 atm. gave XXVI (5 g. as the oxalate). XVIII was prepd. similarly. 5-(.beta.-Hydroxyethyl)iminodibenzyl (13.4 g.) and 6.5 ml. mesyl chloride in CHCl3-pyridine at 0-25.degree. gave 12 g. 5-.beta.-mesyloxyethyliminodibenzyl (XXXVI), m. 130-2.degree.. XXXVI (6 g.) was shaken with 4.25 g. PhCH2CHMeNHMe and 5.3 ml. Et3N in EtOH 8 hrs. to give XXVII (1.2 g. as the oxalate). I, VIII (8 days shaking), XIX, XX, XVI, XXV, and 3-chloro-10-[.gamma.-[(1-methyl-4-diethylaminobutyl)amino]propyl]phenothiazine (di-maleate m. 174-8.degree.) were similarly prepd. Dropwise addn. of 4.68 g. .beta.-(10-phenothiazinyl)propionyl chloride in C6H6 to 2.18 g. PhCH2CHMeNH2 and 2 ml. Et3N in cold C6H6 and after 3 hrs. the mixt. refluxed 1 hr. gave 1.7 g. XXI. Similarly were prepd. XXII, XXXI, XXXII, and XXXIII. V was prepd. from 3-chloro-10-(chloroacetyl)phenothiazine and N-(o-xylyl)piperazine in Me2CO. 3-Trifluoromethyl-10-[.gamma.-[4-(.beta.-hydroxyethyl)-1-piperazinyl]propyl]phenothiazine, b0.2 240-4.degree., was prepd. from 3-trifluoromethylphenothiazine and 1-(.gamma.-chloropropyl)-4-(hydroxyethyl)piperazine. PhCH2COCH2NMe2 (35 g.) in 17% NH3EtOH with H and Raney Ni gave 7.2 g. PhCH2CH(NH2)CH2NMe2, b2 95-100.degree., and [Me2NCH2(PhCH2)CH]2NH, b2 142.degree..

IT **18455-20-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

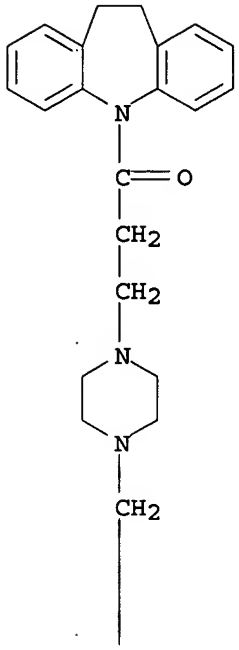
RN 18455-20-4 CAPLUS

CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[3-[4-(o-methylbenzyl)-1-piperazinyl]propionyl]-, fumarate (1:2) (8CI) (CA INDEX NAME)

CM 1

CRN 47724-16-3
CMF C29 H33 N3 O

PAGE 1-A



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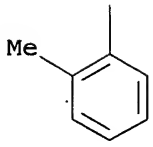
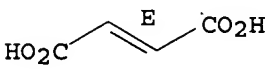


CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



L7 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1964:31000 CAPLUS
DOCUMENT NUMBER: 60:31000
ORIGINAL REFERENCE NO.: 60:5516e-h,5517a-b
TITLE: Antimicrobial imides
PATENT ASSIGNEE(S): Smith Kline & French Laboratories.
SOURCE: 11 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

09/ 076,574

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 932644		19630731	GB	
FR 1344172			FR	

PRIORITY APPLN. INFO.: US 19600815

GI For diagram(s), see printed CA Issue.

AB A number of imido derivs. of 6-aminopenicillanic acid and 7-aminocephalosporanic acid (Ia) are described. The Na salt (I) of cephalosporin C (4 g.) is dissolved in 60 ml. H2O and the pH adjusted to 2.5 by addn. of the acid form of Dowex 50 (x8). The resin is filtered off, washed with 20 ml. H2O, and the combined filtrate and washings are added to 20.5 ml. 0.1N HCl. After 72 hrs. at 20.degree., the mixt. is fractionated over Dowex-1 (acetate form) to yield 7-aminocephalosporanic acid and 3-hydroxymethyl-7-aminodecephalosporanic acid lactone (II). I (1 g.) in 50 ml. H2O adjusted with Dowex 50 (x8) to pH 2.6. the resin filtered off, the filtrate added to 3.8 ml. C5H6N, the soln. kept 48 hrs. at 37.degree., freeze-dried, the residue rubbed with Me2CO, redried, and the residue dissolved in 10 ml. H2O and fractionated as above gave the pyridinium inner salt of deacetylcephalosporin C (III). III subjected to the usual acid hydrolysis yielded 3-pyridiniummethyl-7-aminocephalosporanic acid inner salt. Ac2O (204 g.) and 200 g. 4-chlorophthalic acid heated until the solid dissolved and then for an addnl. 15 min. gave 4-chlorophthalic anhydride (IV). A mixt. of 130 ml. 28% NH3 and 182 g. IV refluxed 1.5-2 hrs. at 300.degree. gave 4-chlorophthalimide (V). To a stirred soln. of 90 g. V, 69 ml. Et3N, and 1 ml. Me2NCHO is slowly added 47.6 ml. ClCO2Et at -5.degree., and the mixt. stirred 30 min. at 0.degree. to yield N-carbethoxy-4-chlorophthal imide (VI). To 30 ml. H2O at room temp. are added 4.32 g. 6-aminopenicillanic acid, 5.75 g. Na2CO3, and 5.06 g. VI, and the mixture is stirred 20 min. to yield 6-(4-chlorophthalimido)penicillanic acid. Similarly were prepd. other 6-imidopenicillanic acids and 7-imidocephalosporanic acids (no phys. data given). Starting with II there was similarly obtained 3-hydroxymethyl-7-succinimidodecephalosporanic acid lactone. Other examples of 7-imido-3-hydroxymethyldecephalosporanic acid lactones were given. Acetylesterase obtained from orange peels is added to 1 g. 7-phthalimidocephalosporanic acid in 15 ml. H2O, and the pH adjusted to 6 and kept at this level for 15 hrs. The soln. is then passed through an IR 4B column (acetate form), eluted with aq. 0.1M AcOH adjusted to pH 5.5 with pyridine, the eluant adjusted to pH 8 with dil. NaOH, and evapd. to yield the Na salt of 3-hydroxymethyl-7-phthalimidodecephalosporanic acid (VII). VII (1 g.) in 10 ml. collidine and 5 ml. EtCOCl is kept 10 hrs. to yield 3-propionyloxymethyl-7-phthalimidodecephalosporanic acid. Other esters were similarly obtained. These compds. have a high resistance to penicillinase and maintain their anti-microbial activity for a prolonged period of time.

IT **2056-38-4**, Ethanesulfonic acid, compd. with 5-[3-(hexahydro-1H-azepin-1-yl)propyl]-10,11-dihydro-5H-dibenz[b,f]azepine
(prepn. of)

RN 2056-38-4 CAPLUS

CN Ethanesulfonic acid, compd. with 5-[3-(hexahydro-1H-azepin-1-yl)propyl]-10,11-dihydro-5H-dibenz[b,f]azepine (9CI) (CA INDEX NAME)

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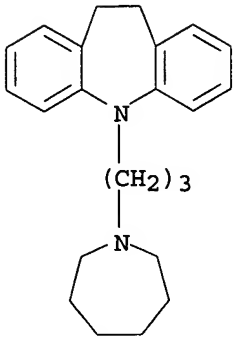
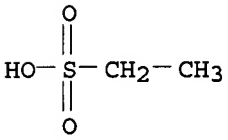
CRN 2056-37-3
CMF C23 H30 N2



CM 2

CRN 594-45-6
CMF C2 H6 O3 S



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L4 12 S L3 AND PROPIONIC
L5 504 S L3 NOT 'BENZO[B,F]AZEPIN'
L6 428 S L3 NOT 'DIBENZ[B,F]AZEPIN'
L7 6 S L6 AND PROPIONIC

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	102.20	251.36
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-11.72	-11.72

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